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BRITISH MEDICAL JOURNAL

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THE FUTURE OF LOCAL AUTHORITY HEALTH SERVICES*

BY

A. LESLIE BANKS, M.A., M.D., F.R.C.P., D.P.H.

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It does not require a very vivid imagination to foresee that during the next few years the British health services are likely to be the subject of searching investigation. No country can afford to go on spending indefinitely one-third of its government's revenue on social services, and the economists have pointed out the dangers. For example, Hagenbuch, in a recent review of the social services, gave the alternatives as "an inflation that at any time may get out of hand and leave us freedom but no security" or "a hurried return to the regime of rationing and controls, with security but no freedom," and, thirdly, "a supreme effort to cut consumption and investment and social services with the minimum of controls. The last is the hardest way and may not be possible. But if it were, it might bring us both freedom and security, not brimming over, but in fairly good measure."[1] When the day of reckoning comes all branches of medicine will be concerned, and indeed from the financial point of view doctors are peculiarly vulnerable.

Some signs of public discontent are already visible. The announcement of the Danckwerts award to general practitioners was swallowed by the public in glum silence. The methods of payment of merit awards to consultants are also open to attack, for these mark a departure from the constitutional principle that the expenditure of public funds must be public. In the words of an annotation in the *British Medical Journal* of February 4, 1950 (p. 295): "As this is public money used to provide pensionable increments to income, has not the public a right to know the names of the recipients? We know of no other public award of money that is kept secret—except the presumed payments to members of the Secret Service." The increases in salaries of medical officers of health have forced the local authorities, much against their will, to raise the salaries of the other chief officers; and, lastly, the disparity between the stipends of clinical professors and the other teachers in the universities has resulted in controversy and dissatisfaction.

The position is a disturbing one, with few precedents on which to rely for guidance. Hasty action by political leaders who feel that they are voicing public demands for full value for money might well result in a rigidly controlled or a full-time salaried service. The only experience on which we can draw is that of the local authority health services. It is difficult to realize how short a time those services have been in existence. Urban and rural sanitary districts date effectively only from 1875 (the Public Health Act of 1848 was an "adoptive" Act). County councils and county borough councils were created by the Local Government Act of 1888 and urban and rural district councils were established as health authorities by the Local Government Act of 1894. Thus our oldest administrative health machine dates back less than 80 years. In those few years it has had to shoulder an extraordinary variety of burdens. At the beginning the pattern of disease with which it was confronted was an appalling one, and the mass of the people were ignorant, illiterate, and indifferent.

In 1852, for example, precisely one hundred years ago, the Registrar-General was gratified to find that "the proportional numbers of men and women who write their names [in the marriage register] is increasing; still, however, 30.5% of men and 44.6% of women sign with marks. And in several counties more than half the women are unable to write their names."[2] In that year, which was a prosperous one, with the "price of provisions low until after harvest, when the price of wheat rose, and potatoes, which are consumed so largely by people of all classes and ages, became dear,"[2] scarlatina caused 18,887 deaths, diarrhoea 17,617 deaths, and typhus, smallpox, and cholera numbered their victims in thousands, as did measles and whooping-cough. Above all there was consumption—"the greatest, the most constant, and the most dreadful of the diseases that affect mankind. It is the cause of nearly half the deaths that happen between the ages of 15 and 35 years."[3] The fact that one mother died in childbirth for every 192 children born alive passed almost unnoticed. Disease and early death were part of the expected order, and curative medicine was almost powerless. On February 13, 1863, the *Medical Times and Gazette* published a letter by Dr. Farr in which he castigated the general hospitals as "ways of death to their inmates" which did not "benefit mankind directly" but merely served as pathological observatories and medical schools.[4]

The field of prevention was wide open to all comers, and voluntary organizations and local authorities buckled to with such good will that by the year 1900 definite improvements had begun to appear, and by 1950 the pattern of disease which the local sanitary authorities had been set up to meet no longer existed. In case this should seem an exaggeration it should be noted than in 1950 scarlet fever caused four deaths in London, diphtheria four, typhoid three, smallpox nil, measles and whooping-cough together 34, and enteritis 64.[5] Typhus and cholera had of course disappeared many years before. In that year (1950) the whole-time staff of the Public Health Department of the London County

*Read in opening a discussion in the Section of Social Medicine and Occupational Health at the Joint Annual Meeting of the British Medical Association and the Irish Medical Association, Dublin, 1952.

Council numbered 7,243, with a gross annual cost of £4,167,204.[6] The London health organization includes also the health services of the 28 metropolitan boroughs, the four metropolitan regional hospital boards, the 26 teaching hospitals, and the general medical services administered by the executive council—a truly formidable machine.

The Swing to Full-time Services

With the turn of this century came a swing from environmental to personal health services actuated partly by fear. In this instance the spur was not cholera or social unrest but the trouncing administered by the Boers in the South African War. The potential soldiers of the Queen were rejected in the proportion of 40–60%.[7] The Interdepartmental Committee on Physical Deterioration reported in 1904 and the school medical service followed in 1907. Here it seems to me that the medical profession made a fundamental mistake in not recognizing the importance of this new service. It is true that the first treatment centre for minor ailments, opened in Hampstead in 1910, had an advisory committee of general practitioners, but it was left to the local authorities to build up a salaried service in which the general practitioner and the hospital consultant played only a subsidiary part. The same comment may be made of the tuberculosis service.

In 1911 the State came openly into this field of clinical medicine because it was recognized that tuberculosis, if neglected, could play havoc with the National Health Insurance scheme. Once again a golden opportunity was lost and the tuberculosis service became a full-time one. So the story continued. Maternal and child welfare, midwifery, mental disease and mental deficiency, the care of the physically handicapped and the chronic sick all became in effect full-time services administered by the local authorities. Meanwhile these authorities were themselves undergoing a remarkable metamorphosis. Local sanitary districts became merged in combined sanitary districts, county councils and county borough councils came increasingly to dominate the local health scene, and under the Local Government Act of 1929 became hospital authorities in open competition with the long-established voluntary hospitals.

It is interesting to speculate on the outcome if that struggle had been allowed to continue, but the comment was soon heard that "regional areas are obviously more suitable for hospital administration than the areas of existing local authorities."[8] The outbreak of war in 1939 saw the introduction of both regionalization and a national (emergency) hospital service. Subsequent developments are so well known that they do not need repetition. To-day we have superimposed on the pattern of local authorities hospital management committees, regional hospital boards, boards of governors of teaching hospitals, local executive councils, and a regional civil service in which each central government department is represented, often with its own medical staff, and, most important, dealing directly with the general public.

Multiplicity of Organizations

We have therefore the extraordinary position that many of our medical services are now administered by bodies on which the locally elected representatives of the people either do not serve at all or are in such a minority that their contributions are not decisive in influencing policy. Indeed, at this stage one may well ask whether local authorities should retain any health services at all. Why not make an all-purpose health and hospital region? It could be said that they have done the work they were set to do and that we cannot afford the luxury of our present multiplicity of organizations. The school-teacher, the bank clerk, and the small trader, hard pressed to live on a few hundred pounds a year, may justifiably inquire why they must continue to support, for example, a medical officer of health, a senior administrative medical officer to the regional hospital board, secretaries to the local hospital management committees and the teaching hospital, all at salaries several times more than their own. There is also a vague and as yet almost unspoken belief that costly hospital and general-practitioner services might well be asked to show more interest in the personal health services which are now the responsibility of the local authority.

On the other side of the medal is the instinctive distrust of powerful monopolies. A regional authority administering health and hospital services, including perhaps industrial medical services, could soon become the object of attack from two opposite sources. The central government departments might regard such an authority with great distrust and do all in their power to curb its growth. The people in the area served would (unless their present apathy continues, which God forbid!) soon protest against remote control and "dictatorship." It seems probable that the pendulum, which has swung violently away from the local authority, would recoil equally quickly from regional control. The alternative of full State control is not one which is likely to be tolerated unless imposed by force or dire necessity. The tradition of local representation is deeply rooted, and it is all the more disturbing to note the trend towards party politics on the national pattern within the local authorities over the past few years. If that continues and expands and the business of the local authority is conducted on the basis of the "party line" instead of local needs it will mean the end of local government as we have come to understand it.

Needs of the Future

When considering the future of local authority health services the best indication is perhaps to ask where the needs lie. But one fundamental question must be answered before this. Do we still believe that the prevention and cure of disease are distinct entities to be retained in separate administrative and technical compartments? If we do then not only must the distinction between local authority and hospital and general-practitioner services be maintained but other new services, such as an industrial medical service, must be established and two kinds of worker, preventive and curative, must be trained. I suggest that the distinction is no longer tenable, and that prevention, diagnosis, treatment, and after-care now form one continuous process, and that we should revise our undergraduate and postgraduate teaching accordingly. If we continue on our present narrow lines of specialization then inevitably gaps will appear in our framework of medical services which will be filled by the layman, and especially the lay administrator and the lay ancillary worker.

That process is already evident in the local authority health services. Environmental sanitation, still a most important part of our health services, is already in the hands of specialists. Purity of water supplies is the responsibility of the water undertaker. Sewage disposal has become an engineering matter. The quality and quantity of food supplies, including milk, are increasingly the concern of the Ministry of Agriculture and Fisheries and the Ministry of Food. The local interests in this matter of purity of food supplies are well served by the sanitary inspector and the public analyst. The control of infectious diseases has ceased to be a matter of concern only to the local sanitary authority. Epidemics are now of national and international importance and require an organization for their prevention and control which oversteps all administrative boundaries. The responsibility for the diagnosis of infectious disease rests increasingly with the laboratory worker, although he is unfortunately not responsible for notification. It is therefore possible for the medical officer of health to remain unaware of the existence of infectious disease in the hospitals in his area for days and even weeks after the laboratory diagnosis has been made—a ridiculous state of affairs.

To question the need for maternity and child welfare services and the school medical service in their present form is to invite a storm of protest and the confident assertion that the facts speak for themselves. Indeed they do. An

infant mortality rate of 26 and a maternal mortality rate of 0.7 show that the years of endeavour have at last borne fruit. They also show that, having defeated the enemy, the great army of workers could now be demobilized, retaining only a highly skilled skeleton staff. These sentiments may be unpopular, but I do suggest quite seriously that the time has come to merge the maternal and infant welfare services with the hospital obstetric and paediatric services.

A similar case could be made for the aftercare of tuberculous and mental patients to be conducted from the hospital rather than by the local health authority.

One other point must be made here. We are no longer dealing only with a population at risk from disease in youth or early adult life, but with a rapidly ageing community. Miss Hornsby-Smith, Parliamentary Secretary to the Ministry of Health, in her address to the Institute of Almoners this year said: "I would remind you that 100 years ago there were nearly 13 people of the working population to every one over 65. At the present time there are only six people of the working population to one old-age pensioner, and by 1977 it is estimated that the figure will be down to four. If I may put it another way: there were a million people over 65 in 1861, and there are expected to be 8,000,000 by 1977."[9] The burden of the chronic sick already presses heavily on the hospitals.

Co-ordination of Local Medical Services

It was not a mere whimsy by the parliamentary draftsman to place local health authority services in Part III of the National Health Service Act of 1946, between the hospital services in Part II and general medical services in Part IV. That was done deliberately, for it was felt that the local health authority could provide the essential link between hospital and domiciliary care. It was also believed that the provision of health centres by those authorities would encourage the development of preventive and curative services under one roof. Restrictions on building have prevented the general provision of health centres, but there is no doubt that much of the distrust of health centres on the part of the general practitioner stems from the ease with which they could lead to a full-time salaried service; for private practice in the health centre might, like the private wards in hospital, be subject to restrictions to be tightened at will, and few men could afford to run private consulting-rooms as well. In the meantime the hospital has become established as the focal point of our medical services, a position that it is likely to retain for many years to come. That the Americans have already realized this is clear from their proposals to make health and hospital regions conterminous. Much of the present suspicion of health centres would be allayed if these could be associated with the hospital, and preferably built within the hospital curtilage, so that the practitioners could call readily on the full range of diagnostic facilities and keep in close touch with the consultants.

The Central Health Services Council has recently submitted to the Minister of Health a report on co-operation in the National Health Service[10] and has recommended that local joint consultative committees should be established for convenient groups of local health authorities, executive councils, and hospital management committees. The area to be covered by a joint health consultative committee is to be called a local health service area. While this recognition of the need for co-operation is valuable it is clear that the committees will be advisory and without power. They can only recommend to the existing bodies. It is to be hoped that these consultative committees may lead to a statutory health and medical care committee administratively responsible for local health services, hospital services, and general medical services. The formation of such an all-purpose health and medical care committee would simplify many matters. It would effect a great saving in secretarial, finance, and records staffs, for at present the health departments, hospital management committees, and executive councils run quite independently. The district nursing service would be more closely associated with the hospital and the general practitioner, and the medico-social workers, health visitor, almoner, and psychiatric social worker would come under one administration. Most important, the position of the medical officer of health would become clear.

The first medical officers of health were clinicians, and if they had been allowed to remain "walking gentlemen with a nose"—that is, physicians interested in the detection and reporting of all matters detrimental to the health of the people—many of our present difficulties would never have arisen. It is most unfortunate that the medical officer of health and the salaried medical officer in central and local government employment were left by their colleagues to play a lone hand for so long, for it has resulted in a dearth of competent medical administrators when they are most needed. Never were Macaulay's words more apt than in this connexion when he said, "It is indeed most important that legislators and administrators should be versed in the philosophy of government."[11] How can we expect others to be versed in the philosophy of government of medicine if we do not ourselves display any interest in it?

The work of the deans of the great medical schools has shown that it is possible for a medical man to be a good administrator. The medical officer of health could play a similar part in the co-ordination of the local medical services if he had the full and active support of his clinical colleagues. An effective first step would be to give him an honorary contract on the staff of the local group of hospitals as home-care physician. It would then be his duty to ensure that all existing resources, and they are many, were used to prevent disease from arising in the individual, to encourage the medical care of patients in their own homes, and, above all, to ensure that the chronic sick do not block valuable hospital beds. He would also be responsible for the co-ordination of aftercare on discharge from hospital. Such an appointment would not trespass on the work of the general practitioner or the consultant, but would be of value to both.

There is no doubt that in the long run any service gets the type of administration it deserves. In the past the medical profession has actively discouraged the medical man who had a flair for co-ordination, and thereby allowed, by default, the lay administrator to take his place. That mattered little when the administrator was in daily personal contact with the medical staff, and indeed the medical profession owes a great debt of gratitude for the help it has had from the house governors of hospitals and the clerks of local authorities. But the fact remains that curative medicine has now followed in the wake of preventive medicine and become a major interest of the State.

Conclusion

The changes in the health functions of the local authorities over the past eighty years have been many. It is not too fanciful to foresee the same process occurring in our medical services in the future. We certainly do not want to see curative medicine develop into the rigidly administered state of the German insurance medical service just before the last war, when even the number of aspirin tablets was dictated. The results of that regimentation are painfully well known to you. Equally we do not want to find ourselves confronted with investigators bent on discovering whether much of the work of the costly clinician could be done by someone with a shorter training and a smaller salary. If the practice of medicine is to be kept at an economic level and at the same time incorporate all the benefits of recent progress, the medical profession must pay more than mere lip service to the adage that prevention is better than cure, for it applies to the health of the medical profession as well as to the health of the nation.

As to method, that was laid down with the greatest clarity by a writer in Dublin more than 200 years ago. Many of you will recall that Gulliver in the course of his travels found, in the Academy of Lagado, a most ingenious doctor, who seemed to be perfectly versed in the whole nature and

system of government and who had somewhat unusual views on the preservation of the health of the body politic. This same doctor, having noted that those in power are often troubled with short and weak memories, proposed that "whoever attended a first minister, after having told his business with the utmost brevity, and in the plainest words, should, at his departure, give the said minister a tweak by the nose, or a kick in the belly, or tread on his corns, or lug him thrice by both ears, or run a pin into his body, or pinch his arms black and blue, to prevent forgetfulness."

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RECENT ADVANCES IN ACTIVE IMMUNIZATION

(DIPHTHERIA, WHOOPING-COUGH, TUBERCULOSIS)*

BY

H. J. PARISH, M.D., F.R.C.P.Ed., D.P.H.

(From the Wellcome Research Laboratories, Beckenham, Kent)

A discussion on active immunization enables us to review advances made in the laboratories of many countries since the war, and also to indicate current trends likely to prove useful to the medical practitioner—surely a main function of the Annual Meetings of the British and Irish Medical Associations. It must be remembered, however, that there is a long incubation period between the conclusion of any new work and the writing of a paper on the subject. Following this there is a long latent period before the article appears in print. Any summary of advances in active immunization cannot ever be up to date, and any statement made to-day may be contradicted to-morrow.

Since chemotherapy and antibiotics are being employed with varying success in the treatment of many diseases, inquiries are naturally made about the future of specific means of control (toxoids and vaccines). In spite of the progress of chemotherapy, immunology has still a very important part to play in prevention and treatment, and there is a need for further research on antigens and methods of using them effectively.

Diphtheria

Since the launching of the national immunization campaign by the Ministry of Health, London, in 1940, the reduction in the toll of this disease in England and Wales has been dramatic. In 1951 diphtheria deaths numbered only 34 (provisional figure) and corrected notifications 699, compared with approximately 3,000 deaths and 55,000 to 60,000 notifications per annum just before the second world war. Fifty years ago there were nearly 10,000 deaths per annum. Moreover, in the past, about 10% of infants might have been expected to suffer an attack of diphtheria and 1% (10% of cases) to die from it (*Medical Officer*, 1951). Where inoculation has been fully practised the toll has been reduced to about 1% of what it was. More convincing evidence of the value of immunization is that the diphtheria notification rate was three times higher and the fatality rate seven times higher over the three years 1945, 1946, and 1947 among non-immunized than among immunized children aged under 15 (Logan, 1952). The chance of a non-immunized child under 15 dying of diphtheria was 22 times as great as that of an immunized child in the same community. These magnificent achievements have not received the attention they merit, because preventive medicine is largely impersonal. The benefit conferred is not appreciated consciously by the person whose life is saved, nor indeed by anyone else. Yet the cost is relatively insignificant both in money and in the trouble involved.

I think we should be careful not to ascribe the improvements in the diphtheria position *solely* to immunization. As is well recognized, scarlet fever and other acute infections have shown a decline in mortality during the last 50 years, although there has been no comparable immunization campaign for their control. Other factors are at work, including, in diphtheria, a possible change in the invasiveness of the causal bacillus. There must be no slackening in our propaganda, but rather an intensification, for there are already in different countries too many susceptible persons, presumably prone to attack by the "enterprising" virulent bacillus we used to know. In a recent review by McGuinness (1952) 30 to 50% of American adults are mentioned as being susceptible. Barr, Glenny, and Parish (1951) examined the diphtheria antitoxin content of 100 samples of cord blood from each of 15 districts of the British Isles; in 10 of the groups, 30 to 59% of the samples contained no detectable antitoxin (under 0.001 unit per ml.). It is obvious that the decline of attendance last year at British clinics must not be accepted with complacency, but be countered by really forceful official propaganda. Mothers who have lost their fear of diphtheria as a deadly illness must not be allowed to remain apathetic.

Not only are there very few cases of diphtheria to-day, but also apparently very few carriers in the general population. Immunization has not increased the number of carriers, as was once thought possible. Thus a paper from Leeds (Bradshaw *et al.*, 1952) stated that no carriers were found in the examination of 6,675 swabs from a highly immunized child community. Other evidence, too, suggests that carrier rates *fall* along with diphtheria morbidity as a result of immunization. This means that, to-day, immunity to diphtheria is less likely to be maintained at a safe level as a result of subinfecting doses of toxigenic diphtheria bacilli. These are so infrequent that we can no longer expect any "boosting" of circulating antitoxic titres from natural immunization. Artificial immunization has therefore taken on an important function, and it must be continued vigorously, endeavouring to conform to good immunological procedures. I have presented the essential principles in convenient form elsewhere (Parish, 1951).

Logan (1952) has stated that the eradication of diphtheria as an indigenous disease in England and Wales can be foreseen as a very real possibility within the next few years. Nevertheless, let us not be overconfident, since the immunity state of the population is disconcertingly low in many areas.

The Prophylactics

All the preparations in use in the world to-day have toxoid or formol-toxoid (French=anatoxine) as their basis; the original highly dangerous toxin has been modified and rendered harmless with formaldehyde, while its capacity to stimulate the production of antitoxin is retained. The fact that unmodified toxin is never used is important, since it precludes any possibility of accident of the type encountered when toxin–antitoxin mixtures were favoured in the U.S.A.

*Read in opening a discussion in the Section of Pathology and Bacteriology at the Joint Annual Meeting of the British Medical Association and the Irish Medical Association, Dublin, 1952.

and elsewhere. Toxoid was used for the active immunization of horses by Glenny and by Loewenstein in 1904 (O'Brien, 1925); it was *not* discovered by Ramon in 1923, as is sometimes alleged, although Ramon was instrumental in having it used on a very large scale for the immunization of French children and soldiers. To-day toxoid is still used on the Continent and in Canada, but prophylactics derived from it are preferred in Great Britain and Ireland. Alum-precipitated toxoid and toxoid adsorbed on mineral carriers give much better antitoxin responses than the fluid antigen.

A.P.T. (alum-precipitated toxoid) has been the prophylactic most used in Great Britain since 1940. I have emphasized that our immunization schemes must be thorough. Better immunity follows the injection of large doses, and there seems to be no good reason why amounts of less than 0.5 ml. (25 Lf) should not be injected into infants. It is worth noting that young children tolerate 0.5 ml. extremely well, although older children and adults sometimes suffer reaction, local and general.

Barr, Glenny, and Randall (1949, 1950) studied the rate of loss of maternally transmitted diphtheria antitoxin in young babies, and found that those with less than 0.04 unit of antitoxin per ml. of their serum could be immunized successfully with two doses, each of 0.5 ml., of A.P.T. These authors also suggested the routine immunization of infants with A.P.T. at 3, 6, and 18 months. In general, the larger the dose used the less the possible interference from maternal antitoxin and the better the response. In younger and lighter babies more antigen was being injected per kg., a point in favour of early immunization. The case for early immunization has received much attention recently in several countries, and I shall refer to it again in the section dealing with combined immunization.

In order to give as good an immunity as possible in routine work it is suggested that: (1) The amounts of A.P.T. injected should always be 0.5 ml. except in older children and adults, in whom 0.2 ml. may be substituted as a preliminary "detector dose" of reactions at the start of the course. As a general rule, a second and final injection of 0.5 ml. is accepted as adequate. (2) In the present state of our knowledge, a single boosting dose at the time of entry to school (Cruickshank, 1952) may be enough for most children who have had a primary course of two well-spaced doses. However, many authorities prefer to give a second boosting dose a few years later. Perhaps a better scheme is to give one boosting dose at 18 months and a second at 4 to 5 years, instead of at 4 years and at 10 years, as is generally advised at present.

T.A.F. (toxoid-antitoxin floccules), which is a weaker antigen than A.P.T., is still used for immunizing adults or those believed to be sensitive to bacillary protein and likely to suffer reaction.

P.T.A.P. (purified toxoid aluminium phosphate precipitated) is used in the same way as A.P.T. It is still undergoing clinical trial. The main point about it is that it contains far less bacillary protein than A.P.T., but it is not known whether absence of bacillary protein is an advantage or a disadvantage in diphtheria prophylaxis.

F.T. (formol-toxoid) has been used both as a crude and as a "pure" or purified preparation. Much research has been directed towards the improvement of toxoid as a basis of all prophylactics. Although so-called "pure" toxoids have been prepared, Pope *et al.* (1951) have found many antigens in them; the composition of diphtheria antigens is more complex than was formerly realized.

Whooping-cough

This is one of the most prevalent and certainly the most lethal of the acute specific infections of childhood. In England and Wales, 9,401 deaths occurred from whooping-cough in the past ten years (Cockburn, 1951). Death is rare in children over 4 years of age; more than 50% of all the deaths are in children under 1 year. Whooping-cough also gives rise to much permanent lung damage from atelectasis and bronchiectasis.

As a clinical attack of whooping-cough gives a fairly solid immunity, successful vaccination has always appeared to be an attainable goal, even in the absence of a simple and reliable laboratory test of antigenicity. Nevertheless, until recently the voluminous literature was so contradictory that scepticism was a common and justifiable attitude to the whole question. But the very persistence of the claims, mainly American, demanded a more critical and better controlled appraisal than this important product had hitherto received.

The British Medical Research Council appointed a committee to go into the matter in 1944, and its interim report (M.R.C., 1951) has shown clearly and conclusively that good vaccines can be prepared. Altogether 7,558 children aged 6 to 18 months were divided into two groups distributed among five different areas. Half the children in the trials received three doses at monthly intervals of various whooping-cough vaccines of British and American origin, and half were inoculated with "anticatarrhal" vaccine as controls. A nurse investigator visited each child at frequent intervals for two to three years, and neither parents nor observers knew to which group each child had been allocated. A total of 3,757 children in the control group produced 687 cases of pertussis by the end of the inquiry, and 3,801 vaccinated children produced 149 cases. The attack rates per thousand child-months of observation were 6.72 among the unvaccinated and 1.45 among the vaccinated, giving a reduction of 78% in the incidence of the disease. Among children exposed to pertussis in their own homes the attack rates were 87.3% of the unvaccinated and 18.2% of the vaccinated group. Further, the cases occurring in the vaccinated were on the average less severe and of shorter duration.

Of the five vaccines tested, two prepared at the Michigan Department of Health were much better than the others, the attack rates in "home exposures" being only 7.3 and 8.9% amongst the vaccinated. Somewhat similar vaccines have now been prepared in Great Britain, and are being studied in laboratories by the Kendrick mouse intracerebral test, and also in various clinics, with a view to determining the value of this novel but promising method of laboratory assay. Field trials of whooping-cough vaccine take a long time, but eventually enough evidence may be produced to justify a national campaign similar to the one introduced for diphtheria immunization by the Ministry of Health, London, in 1940.

In view of the severity and prevalence of whooping-cough in children under 1 year of age, early protection is obviously desirable. Many authorities, particularly in the U.S.A., recommend that the first injection of the course should be given at 2 to 3 months of age, followed by two further injections at monthly intervals. There is no general agreement about the frequency of boosting doses, but until more is known about the reliability of commercial vaccines, one such stimulus per annum till the child is aged 3 to 4 years cannot be regarded as excessive. Moreover, after known close exposures a further dose of vaccine may be advisable.

It is sometimes recommended that mothers should be actively immunized against whooping-cough in the early months of pregnancy. Although high agglutination titres can be demonstrated both in maternal and in cord-blood sera, the protective titres may not be high. At this stage little reliance can be placed on the immunization of mothers as a means of control.

Alum-precipitated vaccines have not hitherto been employed in the British Medical Research Council investigations, but they have been preferred by many workers in the U.S.A., as the alum may possibly have an adjuvant effect in certain types of preparation.

A modified Hornibrook liquid medium (casein hydrolysate, starch, etc.) promises to be satisfactory for the preparation of whooping-cough vaccines on a large scale. The processes of manufacture are simplified, and preliminary reports indicate that the vaccines so produced may be highly potent antigens.

An interesting American development is active immunization with live vaccine (Winter *et al.*, 1952), in an attempt to reproduce artificially the better and more lasting protection conferred by an attack of the disease. The live antigen proved superior to killed vaccine in mouse-protection tests, and its use in human subjects is now under investigation. As *Haemophilus pertussis* is not invasive, it should not cause the actual disease when introduced by any route other than the respiratory tract. The method should therefore not entail undue risk.

Complications of Ordinary Vaccination.—In young children reactions are usually slight, although rather more than after diphtheria prophylactic A.P.T. So-called encephalopathies, manifested by convulsions and other serious nervous symptoms appearing within a few hours or days of inoculation, are rare and may be due to some acquired sensitivity or possibly, in certain cases, to a cerebral vascular accident. As a precaution, any child with a personal or family history of convulsions, and, secondly, any child who has recently had, or is likely to have soon as a result of close contact, any respiratory or other infection should be excluded from vaccination. The association of pertussis inoculations with paralytic poliomyelitis in the inoculated limb is discussed below.

Combined Immunization

The modern trend favours combined immunization in order to reduce the number of inoculations. Moreover, the antigenic response to certain antigens seems to be enhanced.

Diphtheria–pertussis and diphtheria–tetanus–pertussis prophylactics are used on a large scale in the U.S.A. for the immunization of young children. Diphtheria–pertussis prophylactic seems to be less used than formerly in Great Britain on account of the fear of associated poliomyelitis. This combined prophylactic is supposed by many to involve an exceptional risk of the "double event," although the special case against it is still unproved. In this connexion Cockburn (1951) favours the development of combined antigens which do not contain alum, as they should cause less local trauma than other types. A committee is now inquiring into the relationship of paralytic poliomyelitis and inoculations of all kinds. Until the report is published the sensible course is probably to postpone all preventive inoculations during epidemic periods, but the decision must obviously rest with the local health authorities, who have to assess the relative risks of poliomyelitis and of the various infections that may well recur if too much damage is done to the immunization campaigns in the district. Alarmist press reports and correspondence may also have done harm, particularly to the diphtheria campaign, by undue publicity and magnification of the risks.

In view of the high incidence of whooping-cough in the first year of life, some authorities have suggested that the immunizing course of diphtheria–pertussis prophylactic should be begun at 2 to 3 months, as in the case of pertussis vaccine alone. Three doses are generally given at intervals of not less than four weeks, followed by a fourth dose in the second half of the first year of life. There is considerable variation in procedure. Boosting doses may be given at the age of 2 to 3 years and again at 4 to 5 years. Reactions are not worse than would be expected from those observed after each constituent given separately, which means that they are usually negligible in young children.

In concluding this section, I think more attention should be paid to immunization against tetanus, as triple combined prophylactics are feasible. Tetanus toxoid is one of the most effective prophylactics yet developed, and causes so little reaction on injection that immunity is obtained at negligible cost and inconvenience. Many American workers believe that everyone should be actively immunized against tetanus (McGuinness, 1952). Combined antigens—diphtheria, pertussis, and tetanus—have much to recommend them for young children.

Typhoid-paratyphoid vaccine in conjunction with tetanus toxoid (T.A.B.T.) has been used for many years for the Canadian Armed Forces. A recent modification has been the addition of a small amount of diphtheria prophylactic—namely, toxoid adsorbed on aluminium phosphate—following the method of Holt. Three injections of 1 ml. each of the new prophylactic, T.A.B.T.D., are given at monthly intervals, and the indications are that the diphtheria antigen (4 Lf per ml.) does not appreciably increase the amount of reaction (Sellers *et al.*, 1951).

Tuberculosis

As is well known, B.C.G. (Calmette–Guèrin bacillus) and vole-bacillus vaccines consist of living bacteria and produce some degree of active immunity in guinea-pigs and calves in controlled experiments. There is also less well-controlled evidence that they protect man, for whom killed vaccines were found to be ineffective.

B.C.G.

In England and Wales the B.C.G. campaign was begun in October, 1949, using the strain of B.C.G. maintained at Copenhagen (Symposium, 1951). Vaccination was offered to hospital nursing staff, medical students, and contacts of known cases of tuberculosis. The intradermal route of administration was employed. Tuberculin-testing was regarded as an essential preliminary; only those persons who were Mantoux-negative on two tests spaced by six weeks were vaccinated. After segregation for six weeks in the case of adults, or for eight to twelve weeks in the case of children, a third tuberculin test was made. A positive reaction ("Mantoux-conversion") was regarded as an indication that immunity had resulted.

The mortality from tuberculosis has fallen in a number of countries, but there is no scientific proof that it is due to B.C.G. (see, for example, Partenheimer, 1951). In some of these countries, notably Iceland, where the fall has been very great, B.C.G. has not been used at all. The Medical Research Council, London, hopes to get an answer to the problem of the value of B.C.G. within three years.

In Ireland there has been much more enthusiasm for B.C.G. vaccination than in Great Britain. A most energetic attack on the tuberculosis problem at its source has been made over wide districts—for example, in Dublin (Price, 1949) and in County Sligo (Burke, 1951). This magnificent and praiseworthy effort continues.

In the U.S.A. Aronson (1948) reported 55 deaths among approximately 1,500 vaccinated North American Indians; six of these deaths were due to tuberculosis. In the control group, exposed equally to subsequent infection, there were 109 deaths, 53 of which were due to tuberculosis. These results attracted much attention, although they may not be applicable to more civilized communities where genetic immunity to tuberculosis is higher and the risk of infection usually less. Later, Myers (1951) argued strongly against the use of B.C.G. This criticism from a leading American authority raised once again regrets that a controlled study, involving the injection of alternate subjects, was not carried out in man in the early days of B.C.G. vaccination in France. Controlled tests in cattle in the U.S.A. did not show any practical justification for the use of B.C.G. Myers also attacked the Scandinavian claims by pointing out that medical students and nurses who are tuberculin-positive on entry have already passed through the stage of "allergic manifestations." From his own early experience, a small proportion of children and adults had "fever, erythema nodosum, pleurisy, enlargement of hilar structures, and small infiltrates in the lungs"; when these primary complexes subsided the patients appeared well, except in rare instances.

To illustrate his thesis of the comparable risk of tuberculin-positive and tuberculin-negative subjects, he exemplified 160 tuberculin-positive medical students and 145 students tuberculin-negative on entry who later became positive. Of the former group, 3.1% developed reinfection lesions, and

of the latter group 9.6% developed demonstrable lesions. But when the 9.6% of students were analysed further, 6.2% were regarded as primary complexes and pleurisy and only 3.4% as reinfection lesions, a figure similar to the 3.1% of the first group.

The point was also made that B.C.G. has not been proved to be harmless; there have been a number of reports about "Calmette" abscesses and even of pulmonary infiltration. However, Myers's main argument was that there is no justification for taking decreasing mortality as the criterion of the protective power of B.C.G., since similar reductions have been noted in unvaccinated communities. Thus the tuberculosis situations in Denmark and Minnesota showed comparable declines in mortality in recent years, although B.C.G. was used only in Denmark. Myers felt that conventional methods, rather than B.C.G., should get the credit for the improvements in Denmark, as they do in Minnesota. I have already referred to the decline in tuberculosis mortality in Iceland, which was even greater than in Denmark—and took place without any assistance from B.C.G.

In favour of B.C.G. are numerous experiments in animals, which show that immunization with the vaccine retards the development of tuberculosis following *later* injection of virulent tubercle bacilli, and thus results in a more chronic type of infection. This should afford a basis for the hope that in man a resistance should be set up of sufficient duration to support the defences of the body during the danger period when natural infection is taking place. However, Myers maintains that there is no evidence of the development of effective immunity even after an attack of tuberculosis from which a patient has apparently recovered. According to him, parallelism between hypersensitivity and acquired resistance is non-existent: allergic tissues are a prerequisite to the development of the more destructive forms of tuberculosis, the bacilli which were held up temporarily being widely disseminated.

The intradermal method of administration has been most used in Great Britain and Ireland and in Sweden and Denmark, while multiple puncture (with a Hagedorn needle or other instrument) and scarification have been preferred in Norway and France respectively. Newborn infants used to be given B.C.G. by mouth, but this technique is now obsolete. Intradermal vaccination in the deltoid region as soon after birth as possible has recently been employed by Gaisford and Griffiths (1951).

Much attention has been given recently to the method of preparation of the vaccine. "Liquid vaccine," which is the type ordinarily used in Great Britain and Ireland and in Scandinavia, has a very short life—only ten days or so from the date of preparation. (This and other traditional concepts about B.C.G. vaccine and vaccination have been challenged recently by Palmer (1952), of the Tuberculosis Research Office, W.H.O.) Freeze-dried vaccine should retain full viability and immunizing efficiency for many months. The workers at the Pasteur Institute, Paris, have been outstanding in developing a dry vaccine.

My own views in this difficult field of vaccination against tuberculosis may be summarized as follows. While the value of B.C.G. in man has not been proved, it is sounder preventive medicine to produce primary allergic complexes with a living attenuated vaccine, even if its complete innocuousness is occasionally in doubt, than to risk the potentially dangerous manifestations that may result from random natural infection with virulent bacilli. The essence of all vaccination procedures is to produce some immunity with antigens, living or dead, that are safer than an attack of the natural disease. One recollects that, in the case of smallpox, variolation was replaced by vaccination, and that Pasteur's attenuated virus is used in the prevention of rabies. But it is also noteworthy that in the attack on tuberculosis "fundamental control measures" have often produced considerable falls in mortality without any part being played by B.C.G. At best, B.C.G. must be regarded as an adjunct to, and not as a substitute for, precautions introduced to prevent frequent or massive exposure to infection. Unfortunately in many countries to-day the injection of B.C.G. is the only measure of control which is practicable.

Wells's Vole Bacillus (Living)

This is the only tuberculosis vaccine which competes at all with B.C.G. It consists of a culture of a strain of murine tubercle bacillus, and has the advantage over B.C.G., an artificial laboratory product, that it is already stabilized in its virulence for man and cattle. Attenuation from prolonged and repeated subculturing is thus unnecessary. Although some results in guinea-pigs, cattle, and man are encouraging, it is unlikely that Wells's vaccine will ever oust B.C.G., or even offer a serious challenge to it, if only because B.C.G. is already well established.

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FOUR CASES OF OBSTRUCTION AT THE DUODENO-JEJUNAL JUNCTION

BY

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Unusual cases tend to come in runs, and sometimes present such similar features as to enable those who have encountered them to suggest the diagnosis in subsequent cases with reasonable certainty. During the past year four such cases have come our way—namely, obstruction at or near the duodeno-jejunal junction resulting from narrowing by growth. Two were caused by primary carcinoma of the duodenum, one followed infiltration by carcinoma of the body of the pancreas, and one followed infiltration by some adenopathy of adjacent glands. Each case presented points so strikingly alike that the syndrome could be recognized as pointing to some stenosis at or just beyond the junction.

Case 1

A minister of religion aged 39, a married man with one child, had been in robust health until six weeks previously. He was then on holiday, during which he began to suffer epigastric pain some 10–15 minutes after meals. It lasted about an hour, was unrelieved by alkalis, and did not radiate in any direction. Within a few days he began to vomit copious amounts of dark-green, watery, bitter-tasting fluid. This vomiting was quite unrelated to food, and he declared that pints of fluid just flowed from him. He was put on a milk diet, and remained on it until admission to hospital.

The vomiting was checked somewhat thereby, but still occurred once or twice each day; it never contained blood. The pain ceased one month after the onset. He had lost weight. The bowels were constipated, but the stools were pale as the result of the milk diet. He was a non-smoker and teetotaller.

On admission under Dr. Trevor Cooke his general condition was found to be reasonably good, there being no complaint of pain, no dehydration, no abdominal swelling, tenderness, or free fluid, and no abnormality being discovered in any other systems of the body. The fasting test meal showed charcoal in all specimens, fasting juice of 182 ml., and residual juice of 308 ml. Starch and bile were present in all specimens, but no blood. Serum chlorides were somewhat low, being 233 mg. per 100 ml. Blood counts showed R.B.C. 5,890,000, Hb 120%, C.I. 1.02—the result of a mild degree of haemoconcentration.

At this stage I was asked to see him. The condition was regarded as one of high intestinal obstruction, and after rectifying the chloride deficiency it was decided to explore.

First Operation (October 1, 1951).—This was done through a right paramedian incision. In the region of the duodeno-jejunal junction was a hard mass, the size of a golf-ball, obstructing the duodenum and causing considerable distension of its more proximal part. On the surface of the bowel at the site of the swelling were small nodules of carcinoma invading the lymphatics, and there were hard glands in the upper part of the mesentery. The tumour was straddling and adherent to the aorta, and was obviously irremovable. An anterior gastro-enterostomy was therefore performed at about 8 in. (20 cm.) from the junction, this distance being chosen with the hope of being beyond the diseased bowel, and the abdomen was closed in layers.

Progress.—Careful watch was kept on fluid and crystalloid balance, and by means of a mixture of saline, glucose, and Hartman's and Darrow's solutions this was maintained. However, vomiting continued intermittently, and it became obvious that the stoma of the anastomosis was not working properly. It was therefore decided to reopen the abdomen.

Second Operation (October 13).—The abdomen was opened through the original wound. A little free fluid was present. The efferent loop of the gastro-enterostomy was adherent to the back of the first wound; it was thickened and dilated, but there was no mechanical obstruction. The efferent loop was opened, and with a finger the stoma was explored and found to be patent. The afferent loop was also explored, and on its posterior wall, just at the termination of the duodenum, was felt a small ulcer crater with hard edges, but it could not be brought into view. The jejunal incision was sutured and the abdomen closed in layers.

Progress was promising for 24 hours, but the patient then developed a rigor, collapsed, and died at 5.30 a.m. on October 15.

Post-mortem examination revealed a carcinoma of the body of the pancreas invading the last part of the duodenum.

Case 2

A married woman aged 59 was admitted under Dr. Trevor Cooke. She had been perfectly well until two months before when she suddenly vomited one to one-and-a-half hours after a meal. There was no discomfort other than a feeling of heaviness, but from this time onwards she vomited frequently, usually in the evening. The vomit was copious, and often contained food taken 12 hours previously, and also bile. The longest spell of freedom during these two months had been a fortnight, and at its worst the vomiting was at least once a day. The appetite had become poor and she had lost weight. Latterly she had less energy, had noticed herself becoming pale, and had become breathless on exertion. Mr. B. N. Brooke was asked to see her.

On examination a mass could be felt in the left hypochondrium which did not move much with respiration. No other abnormality was found in the abdomen, and the rectum and pelvis were clear. R.B.C. 3,690,000, Hb 48%, C.I. 0.65, W.B.C. 4,900. The cardio-respiratory and renal systems were normal. A barium meal showed a 24-hour residue; the second part of the duodenum was dilated, the first part not seen, and it was suggested that a chronic duodenal ulcer was responsible. The report on a second barium meal taken five weeks later stated that no definite ulcer was seen, but that there was a diverticulum of the second part of the duodenum. A fractional test meal revealed achlorhydria, which was unaltered by histamine or insulin, and nearly all specimens contained bile.

Operation (January 2, 1951).—It was decided to explore, a pyloric neoplasm being thought to be the likely lesion. After the usual preparation this was carried out by Mr. B. N. Brooke; the following is his operation note.

"Through a right upper paramedian incision a tumour about ¾ in. (1.9 cm.) in diameter was felt in the third part of the duodenum. It was hard, like carcinoma, and there was a gland between the duodenum and head of the pancreas. The duodenum was divided distal to the tumour and the distal end closed in three layers. The duodenum was also divided proximal to the tumour, and the part containing the tumour was removed. The stump of the proximal duodenum was anastomosed to a loop of upper jejunum brought up in front of the transverse colon."

Convalescence was uninterrupted. The pathological report was: "(1) Portion of duodenum invaded on its external surface by well-differentiated adenocarcinoma. Histological character resembles that of a tumour of the large bowel rather than intrinsic duodenal growth. (2) The lymph node shows no evidence of metastatic involvement."

Case 3

A man aged 62 was admitted as an emergency case under Dr. E. Bulmer on December 7, 1951. Until nine days previously he had been in perfect health, but then developed severe epigastric pain after a public dinner, and 12 hours later he began to vomit, this continuing right up to admission to hospital. Both solids and fluids were returned almost immediately after swallowing, and the vomit contained bile but no blood. On admission he was constipated and thirsty.

On examination he was found to be a restless, alert, and intelligent man of good physique. The tongue was dry. There was guarding in the left hypochondrium, but, apart from this and a palpable left colon, nothing was discovered in the abdomen. The rectum was normal, the prostate slightly enlarged. There was severe dehydration, and the blood urea was 146 mg. per 100 ml. The serum chloride ion was 286 mg. per 100 ml.

On a regime of gastric suction and intravenous fluids his condition greatly improved, the blood urea being 52 mg. per 100 ml. and the serum chloride ion 315 mg. per 100 ml., and after two days he seemed in every way so much better that the gastric tube was removed, the intravenous drip was discontinued, and fluids by mouth were allowed. Within a few hours he vomited 22 oz. (624 ml.) and on the passing of another Ryle's tube a further 52 oz. (1,474 ml.) was aspirated from the stomach and bile was present. Intravenous saline and glucose was restarted, and the general condition further improved, serum chloride ion rising to 366 mg. per 100 ml.; proteins were 5.6 g. per 100 ml. However, stomach aspirations continued to exceed intake by mouth. It was assumed that there was a high small-intestinal obstruction, and because of its similarity to the two previous cases I ventured to place it at about the duodeno-jejunal junction.

Operation, on December 15, proved this correct, and a small stenosing carcinoma was found involving the last inch (2.5 cm.) of the duodenum. The growth was infiltrating the peritoneal coat, but there were no palpable glands and no secondaries in the liver. The duodenum was divided 1 in. (2.5 cm.) proximal to the upper end of the growth, and the jejunum 8 in. (20 cm.) below the junction, the proximal end being anastomosed to the front of the second part of the duodenum. The specimen contained a small mass of

fat from the back of the duodeno-jejunal junction, a few tiny glands being included therein. The pathological report reads: "Adenocarcinoma of jejunum, with mucoid change in the deeper portions. Penetration of the bowel is complete. A small lymph gland shows no secondary invasion."

Convalescence was satisfactory, and he remains well.

Case 4

A bus-driver aged 35 had been in hospital a year previously under Professor Melville Arnott with thrombophlebitis migrans, which led to thrombosis of the superior and inferior vena cava; no satisfactory explanation had been found for this.

On April 11, 1952, he was readmitted under Professor Arnott, this time as an emergency case. He said that since his previous spell in hospital he had been perfectly well until a month previously, when he began to suffer epigastric pain, which went through to the back and was colicky in nature. It was unrelated to meals, and was relieved by heat and "veganin" tablets. Alkalis were ineffective. He began to vomit four days before, at first in small quantities, but then in larger amounts. The vomit was yellow, and on admission occurred every half-hour. On the day of admission the vomit was darker brown, and contained a little blood. With the onset of vomiting the pain became easier. The bowels had acted regularly each day, including the morning of admission.

The patient did not think he had lost any weight, though his appetite had become poor. He regarded himself as cured from the former thrombosis trouble, having been at full work since then, and had not noticed any swelling of arms, legs, or face. However, he became breathless on exertion and admitted to some swelling of the face after walking more than 200 yards.

On examination he was thick-set and looked ill, flushed, and anxious, and he vomited coffee-ground material frequently during the interview. Temperature 99.8° F. (37.7° C.) and pulse 80. Micturition and urine were normal. In the epigastrium was a tender rounded mass transmitting pulsation. The liver was enlarged to three fingerbreadths below the costal margin. Neither spleen nor kidneys were palpable, and no abnormality in the pelvis was found on rectal examination. The axillary glands were enlarged. The neck veins were full, but no other abnormality of cardiovascular or respiratory systems could be found. The testicles were normal.

At this stage I was asked to see this man, and did not feel I could be more precise than to say that he had high intestinal obstruction and required laparotomy; but I remarked to one of my team that the case reminded me of the three cases described above.

Operation (April 13).—The abdomen was opened through a left paramedian incision. The lump previously felt on examination was found to be a retroperitoneal mass, which on closer examination proved to be part of a gross generalized intra-abdominal adenopathy. The glands along the aorta and both iliac arteries were enlarged and fused together, as also were those in the mesentery, mesocolon, and mesosigmoid, and there was a further mass in the hollow of the sacrum to which the rectum was tethered. In the region of the main mass—namely, behind the stomach and duodeno-jejunal junction—the peritoneum was puckered, giving the appearance of being infiltrated by growth, and the transverse mesocolon was so shortened thereby that the colon was drawn right back on to it. In the same way the duodeno-jejunal junction was affected, but, so far as could be detected, there was no involvement of the stomach wall itself. The effect of this adenopathy was therefore to narrow the duodeno-jejunal junction considerably. An anterior gastro-jejunostomy was performed as a short-circuiting device. No secondary deposits could be felt in liver or spleen. A gland from the mesentery was removed for biopsy. The patient made an uninterrupted recovery.

The report on the mesenteric gland was that there was no evidence of neoplasia, but marked inflammatory hyperplasia with sinusoids distended with reticulum cells. Because of this somewhat unsatisfactory explanation of his illness, glands were removed from each axilla, but precisely the same appearance was reported.

He was discharged home on May 14 in excellent condition, and has since remained so.

Conclusions

The outstanding features of these four cases are: (1) a short history—a matter of weeks only—of epigastric discomfort or pain; (2) the onset of vomiting very shortly afterwards; (3) the vomits contained bile in all four cases; (4) in all four the symptoms were those of high small-intestine obstruction of a subacute nature.

The short history and fairly sharp onset were against pyloric stenosis from ulcer or neoplasm, and so, too, was the presence of bile in the vomits and the fractional test meal. The absence of collapse from severe colic was against acute obstruction of the small intestine, but the copious and oft-repeated vomiting, together with dehydration, pointed to partial obstruction at a very high level. That several mechanisms may lead to such partial obstruction is shown by these four cases.

THE MANAGEMENT OF CHILDREN WITH PRIMARY TUBERCULOSIS*

BY

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To guide a patient satisfactorily through any illness we must be thoroughly familiar with the natural history of the disease and the possible variations of its course, particularly those dependent on the age and circumstances of the patient. In this paper we deal with the child who has his first infection with tuberculosis—that is, with a primary tuberculous focus and the accompanying tuberculous adenitis of the regional lymph nodes.

What advice should be given concerning the child with the primary tuberculous infection? How does the advice accord with the stage of the infection, the age of the child, and the circumstances in which he lives? These are the practical questions of medical practice, and to answer them we must know the natural history of the disease. It must be confessed that in spite of the vast expense and labour involved in the study of this disease process there are great gaps in our knowledge. Many of the fundamental features of the natural history of the primary and post-primary infections are still unknown.

Natural History of Primary Tuberculosis

Nine out of every ten of our population undergo a primary infection with tuberculosis before the age of 20. The entry of the tubercle bacillus into the lungs

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with the formation of a primary focus takes place, in 80–90% of those infected, after contact with an infective adult. In the remainder, it occurs in the abdomen, in the nasopharynx, or on the skin. Wherever the site of the initial infection, whether it be visible as in the skin or invisible as in the lungs, a small tuberculous lesion appears, and the neighbouring lymph nodes enlarge.

The primary complex often forms without any disturbance of general health, and usually both the focus and the glands are painless. In an unknown proportion of children there is, however, about two to four weeks after infection, a general febrile reaction, with malaise and sometimes joint or muscle-aching, but without other abnormal clinical signs unless sensitivity reactions such as erythema nodosum or phlyctenular conjunctivitis occur. If the regional glands are visible in the neck or axilla or groin, as they may be from about 14 days after infection from a neighbouring primary infection, they may become tender and may indeed simulate an acute pyococcal infection. If in the abdómen, they may form a palpable mass and give rise to pain. Whether or not there is a febrile reaction, the body becomes sensitive to tuberculo-protein about four to six weeks after infection, and this altered sensitivity is turned to diagnostic or epidemiological use in the various tuberculin tests.

This febrile reaction, or " fever of onset," settles within a month ; if it be prolonged thereafter we should suspect either extension of the primary focus or the beginning of disseminated disease. For the real immediate danger of the primary infection is that in a small proportion of cases, varying with age, with inborn resistance, possibly with nutrition and intercurrent infection, widespread dissemination of the tubercle bacilli will give rise to miliary tuberculosis or tuberculous meningitis. In others, again an unknown proportion of those infected, though widespread and overwhelming infection does not ensue, localized complications occur : in the lung there may be bronchial erosion or occlusion, or pleural effusion ; in the body, lesions in bones or joints. These complications, widespread and local, are most likely to arise in the first two years after infection, the risk diminishing afterwards. Fortunately, though we do not know the proportion of children who develop other tuberculous lesions after primary infection, we can say that in the majority the primary complex is healed and either disappears or is calcified. Once this has taken place the child seems to enjoy a period of relative safety from tuberculosis until young adult life brings the risk of localized chest lesions of " bronchogenic " or " adult " type—lesions arising either by reactivation of bacilli derived from those causing the primary infection or by new bacilli introduced from outside.

In this outline of the natural history of the primary infection there are certain important gaps. We know that dissemination is most likely to occur in children infected in the first two years of life, but we do not know the risk of dissemination at different ages and under different conditions ; we do not know which individuals are likely to develop miliary tuberculosis or meningitis.

We know that we shall be asked for advice under two very different conditions. First, there is the child who is clinically ill ; secondly, there is the child with a primary complex in the chest discovered in a routine examination at school, as a tuberculous contact, or in the course of investigation for some other condition. These two groups of children present quite separate problems.

Asymptomatic Primary Pulmonary Tuberculosis

When such a child is found what do we recommend ? Should we advise treatment at home, or in hospital ? Is active treatment necessary, or should we wait and see ? Our attitude to these questions must depend upon our estimate of the chance of the development of clinical illness and, more particularly, of dissemination. We therefore need to make a numerical estimate of the risk of dissemination. Such an estimate is only possible for a given population when the conditions for study are favourable. But they are so fundamental that I wish to give the estimate which Dr. Cammock and I have recently made for children infected under 5 years of age in Newcastle-upon-Tyne.

The study in which this estimation was made is still in progress, but, very briefly, we have been able to trace the tuberculous history of all the children under 5 years of age in Newcastle on December 31, 1949. We have been able to estimate that 1,200 of the 25,000 children under the age of 5 would have undergone or be undergoing primary infection—ranging from 2% of those under 2 years to 10% of those in the fifth year of life. In Newcastle, such ill children reach hospital, and we have had help from the staff and access to records of all children's units.

From January, 1945, to December, 1951, 41 of the 25,000 children who would still have been under the age of 5 in December, 1949, developed tuberculous meningitis or miliary tuberculosis, or both. The risk of a child developing tuberculous meningitis or miliary tuberculosis is therefore about 1 in 30, or 3%. This is almost certainly the period of greatest risk. Over this age, during the school years, the chances are probably less, but as a matter of urgency we need to know the risk of primary infection in both school years and adolescence.

The next question we ask is, Knowing the risk of dissemination in untreated cases, can we design an experiment to prove that treatment will alter the likelihood of dissemination ? With a risk of 3% and a treatment 100% effective we would need at least 300 children under the age of 5 years with a known recent primary infection before the result would be likely to be statistically significant ; with a remedy 50% effective the group would have to be doubled. It seems, therefore, very unlikely that the conditions for such an experiment could be realized. Thus we have not as yet, and for a long time to come we will probably not have, the data to determine the results of treatment of the asymptomatic primary tuberculous complex.

At the present time, therefore, with the possible exception of the very young infant, I do not recommend chemotherapy for the well child who has a pulmonary primary infection. Nor do I, except where the child's home is quite inadequate to provide proper care and attention, advise hospital or sanatorium treatment, for I believe it is particularly desirable to keep young pre-school children at home, or at least in a family where they can feel secure.

Is there, then, anything we can do for the child who has recently undergone infection but remains well ? I believe a great deal can be done. We can see that he receives adequate food and sleep and otherwise lives a normal life, even to attending school. Intercurrent infections must be promptly treated, but above all we must always be alert for the insidious changes which denote *early* tuberculous meningitis or miliary tuberculosis. Prognosis now in these conditions depends more than anything else upon the length of time between onset and diagnosis. Diagnosis depends upon the early recognition of change of habit or health in a previously well but infected child. Vomiting without obvious cause repeated for more than two or three days, refusal of food, and irritability are signs to look for ; in the older child headache should raise our suspicions, or in the case of miliary tuberculosis an unexplained pyrexia or loss of weight. The complications will be diagnosed from the history (often a history of contact with adult infection can be obtained), and from knowledge of previous tuberculin conversion, confirmation will be obtained by

lumbar puncture or radiology. For the family doctor, however, the key to the situation is the use of the tuberculin test in the children in his practice.

Treatment of Children Ill with Pulmonary Primary Tuberculosis

In the treatment of children ill at the time of primary infection, or with local complications later, advice is required on the necessity for rest, whether that rest should be at home or in hospital, and whether streptomycin and *para*-aminosalicylic acid (P.A.S.) should be used.

The commonest clinical manifestations of the primary complex are the initial fever with malaise, and limb and joint pains simulating and often mistaken for rheumatism; the child loses appetite and weight, and sometimes the skin becomes peculiarly dry and coarse. The spleen may be felt, though it is seldom greatly enlarged. After confirmation of the diagnosis and the taking of radiographs the child may be kept at home in bed if the home conditions are adequate. The fever of onset does not usually last longer than a month, and, provided a close watch is kept for any sign of dissemination or the development of meningitis, it is not our custom to use antibiotics at this stage. If, however, the pyrexia should continue for six weeks even in the absence of any radiological evidence of dissemination, streptomycin and P.A.S. should be considered. If the home is inadequate then hospital or sanatorium treatment may be necessary, and, in any case, careful supervision with radiological control for at least the next two years is required. In this period the family doctor's appreciation of the situation and his recognition of apparently minor deviations from normal are all-important, for he is likely to be the first person to see the child unfortunate enough to develop miliary tuberculosis or tuberculous meningitis.

Primary Infection in Very Young Infants

There seems to be no doubt that the danger of primary tuberculous infection is related to age, and that primary infection during the first year of life is much more likely to give rise to clinical illness and to disseminate than infection after that age. Infected infants must therefore be kept under very close supervision indeed. The three most important guides are weight, temperature, and behaviour—especially refusal of feeds—irritability, or vomiting. If there is either fever or weight loss my practice is to recommend admission to hospital and administration of intramuscular streptomycin and P.A.S., even if there are no clinical or radiological signs of spread. The effect of this therapy on a child who is febrile and losing weight is sometimes, as in Case 1, most convincing. We have no fixed period for the course of therapy, the duration being judged on clinical improvement.

Case 1. Febrile Primary Tuberculosis Without Visible Dissemination

A male infant aged 8 months had been in constant contact with two tuberculous uncles. The first child in the family had died with tuberculous meningitis 18 months earlier. In November, 1950, the patient became irritable and off colour, and remained so until his admission to hospital on January 31, 1951. On admission he was thin and flabby, weighing only 14 lb. (6.4 kg.), with a fever up to 100° F. (37.8° C.) each evening. The tuberculin reaction was strongly positive and a radiograph showed a primary complex in the left side of the chest, but the cerebrospinal fluid was normal and there was no sign of dissemination. For three weeks he ran an irregular fever, unaffected by sulphonamide or penicillin. On February 21, for the first time, a few rales were heard at the base of the left chest, and a further radiograph showed that the primary focus was larger. Streptomycin was now started, and although at first the child continued to lose weight, his temperature settled and he rapidly became playful and happy. It was not until one month after the beginning of treatment that he had a reasonable gain in weight, but thereafter he steadily improved, gaining 2½ lb. (1.1 kg.) in the next seven weeks. He had 0.5 g. of dihydrostreptomycin (which at that time we were using) daily for three months. At the time of writing he is well, with a well-calcified left-sided primary complex.

Bronchial Complications of the Primary Infection

Local complications causing illness are an extension of the primary focus itself, bronchial erosion with aspiration of infection, or bronchial occlusion by granulation tissue and caseous material.

Bronchial Occlusion

Complete bronchial occlusion is sometimes only a transient phenomenon, seemingly due to simple pressure of enlarged glands on the bronchial wall. But a much more troublesome type of occlusion is produced by extension of the tuberculous process from the gland and erosion of the bronchial wall, which then is wholly or partly filled either by tuberculous granulation tissue or by caseous material, or a combination of both.

If at first the obstruction is incomplete the lobe or segment beyond becomes emphysematous, but if it fills the lumen then absorptive collapse results. Sometimes there is in addition an inflammatory change also within the collapsed area. This process slowly heals, and as it does so the bronchus becomes stenosed or distorted and the lung scarred, so that the final result is bronchiectasis. Everyone with experience of primary tuberculosis is familiar with these cases. As a rule the children have a cough, which may be hard and spasmodic if there is much bronchial irritation, or loose and productive if secondary infection has already occurred. It is in these cases that bronchoscopic removal of granulation tissue or a mass of caseous material seems to hold out hope of reopening the bronchus to allow air to enter the lung beyond. In my experience, however, it is only in the exceptional case that the lobar or segmental shadow disappears after bronchoscopy. Two possible reasons for this are that in many cases the obstruction is too far down the bronchial system to be reached by the bronchoscope, and that the segment of lung beyond is consolidated. We have therefore turned to streptomycin in the hope that by healing the granulations and assisting the absorption of pneumonic processes the lobes can be re-aerated. Here again my own experience, and that of Hutchison in Glasgow (personal communication, 1952), has been very disappointing, and we have rarely seen the re-expansion of a collapsed lung following streptomycin therapy, and "collapse" shadows not infrequently appear during the treatment of miliary or meningeal tuberculosis.

The most likely reason for this failure is that caseous material in the lumen of the bronchus remains unaffected by streptomycin, and at the same time may provide a continuing source of infection of the lung beyond. When, however, the obstruction has been removed, streptomycin will assist in the absorption of the inflammatory reaction in the lobe.

Case 2. Resolution of Aspiration Pneumonia After Coughing of Caseous Gland

A small delicate boy aged 2 years 11 months was admitted on April 16, 1951, with a history of three weeks' slight but persistent cough, with loss of energy, appetite, and weight. On examination he was seen to be an ill-looking fretful child, with alae nasi working, rapid breathing and generalized wheezing. His temperature was 103.4° F. (39.7° C.). Numerous coarse scattered rales and rhonchi were heard in both lung fields. The tuberculin test was positive. At first his temperature settled with penicillin therapy, but as the secondary infection subsided there was a constant diminution of air entry at the left base. Over the next week he became more lively, but thereafter the temperature rose and he became listless again, with a troublesome cough and sweating.

FIG. 1.—Case 2. Mass of caseous material coughed up.

During the next 24 days his general condition remained poor, and on May 15 he had a sudden spasm of coughing and brought

up a large mass of caseous material measuring 1¼ by ¼ in. (3.2 by 1.3 cm.) which on histological examination contained tubercle bacilli and many secondary micro-organisms (Fig. 1). After this incident he was acutely ill and the radiological shadow at the left base increased (Fig. 2). Streptomycin therapy was started; thereafter he improved, to make a complete recovery, the consolidation in the left lower lobe disappearing (Fig. 3). We do not yet know if any stenosis of the bronchus remains.

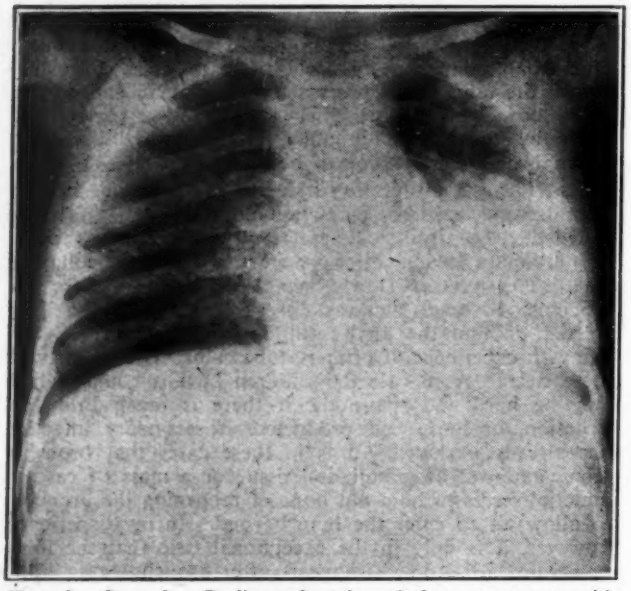

FIG. 2.—Case 2. Radiograph taken before treatment with streptomycin.

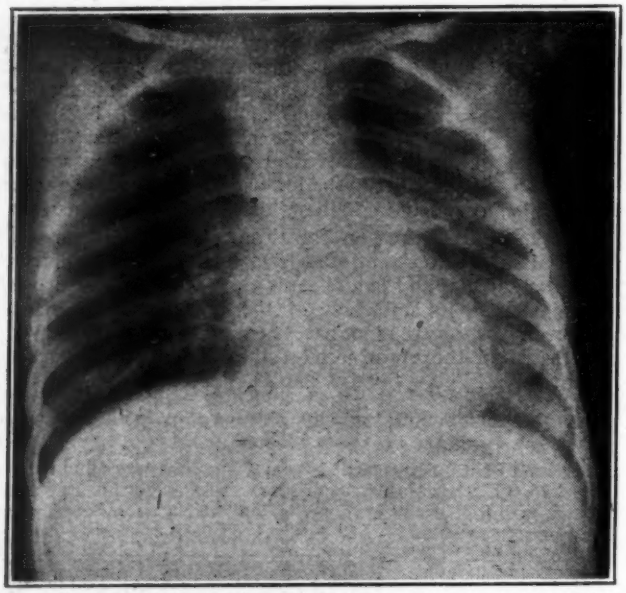

FIG. 3.—Case 2. Radiograph taken after treatment with streptomycin.

Bronchial Ulceration Without Occlusion

Occasionally the tuberculous process in the regional lymph nodes erodes the wall of the bronchus, forming an ulcer draining a gland. There is no blocking; instead, bacilli and fragments of caseous material are drawn into the lung beyond, forming small areas of tuberculous bronchopneumonia. These cases, though infrequent, are important; for, as shown in Case 3, they will respond to streptomycin.

Case 3. Ulceration of Bronchus, with Tuberculous Bronchopneumonia

A girl aged 4 years was admitted to hospital on December 10, 1947, complaining of pain in the back and lassitude for one month. Crepitations had been heard over the left lung anteriorly and posteriorly, and she had failed to respond to chemotherapy at home. After her admission the tuberculin test was strongly positive, and radiological examination showed patches of inflammatory reaction throughout the left lung. Streptomycin, 0.5 g. daily, was started two days after admission. Tubercle bacilli were demonstrated in the gastric contents, and 12 days after admission bronchoscopy revealed an ulcer with raised swollen edges in the left main bronchus, 1 in. (2.5 cm.) from the carina. Histological examination of material taken from the edge revealed the tuberculous nature of the process.

Throughout January, 1948, there was a steady gain in weight, but at the beginning of February the lesion in the bronchus was still present. Streptomycin, which had been stopped for two weeks, was restarted, and improvement continued all the month, and in March there was visible improvement in the *x*-ray films. On April 9 the third bronchoscopic examination showed only a local reddening of the wall of the bronchus where the ulcer had been. In another week the patient was running about happily, and the last streptomycin was given on April 22, the total dosage having been 50 g. She was discharged home on April 30 and has remained well ever since.

Without streptomycin therapy this child would almost certainly have developed a progressive tuberculous bronchopneumonia of the whole of the left lung.

Treatment of Primary Infection Outside the Lung

Although about 90% of cases of primary infection occur in the lung, there remains an important group in which infection occurs either in the abdomen or in the skin or other mucous surfaces, especially those of the nasopharynx or tonsil, giving rise to a primary focus, the regional glands appearing in the neck.

Under urban conditions the abdominal primary infection is becoming uncommon, and the ascitic or plastic abdominal peritonitis is not often seen. Recently the most common manifestation of abdominal tuberculosis seen in our department has been in children with illnesses simulating an acute abdominal emergency, and the diagnosis has been made at laparotomy.

Case 4. Abdominal Tuberculosis Simulating Appendicitis

An only child, aged 5, of a good family living in an unsuitable house was admitted to hospital in December, 1950, with a history that three weeks earlier she had had measles followed by spasms of lower abdominal pain, two or three attacks each day and occasionally at night. She had not vomited and had been rather constipated. Two days before admission, at 6 p.m., while sitting in front of the fire, she had an attack of unusual severity lasting five minutes, and thereafter complained of pain on moving the right leg. The next day she was weary, and in the evening the abdominal pain began again, becoming severe on the right side.

On admission her temperature rose to 99° F. (37.2° C.), and pulse 110. In the abdomen there was marked tenderness and some guarding, but on careful palpation a mass was felt in the right iliac fossa. The summary of the history was unlike appendicitis, but the tender lump and guarding made laparotomy necessary.

At operation a large mass of caseous glands was found in the ileo-caecal region with a few small tubercles over the surface of the bowel. Intramuscular streptomycin was started, and the temperature, which reached 101° F. (38.3° C.) on the day after operation, fell to normal within 10 days. Streptomycin, 1 g. daily, was given for five weeks; the mass steadily diminished in size and the blood sedimentation rate fell from 35 on December 16, to 18 on January 2, 1951. In the next three months she gained 11 lb. (5 kg.) in weight.

My impression is that the streptomycin helped to bring about a more rapid recovery and diminished the reaction about the glands more quickly than would have been accomplished by rest alone.

Tuberculous Lymphadenitis in Neck, Groin, and Axilla

It is likely that the appearance of a large tuberculous gland surrounded by a zone of smaller satellite glands indicates that this particular gland, whether it is in the neck, axilla, or groin, is the regional gland of a primary complex in a neighbouring area drained by the glands. Careful search of the mucous membranes or skin in the area drained by the gland will sometimes reveal the focus.

Indeed, in five years I have seen more than 30 cases in which I have been able to demonstrate the primary focus in the skin, mouth, or eye in relation to the regional lymphadenitis.

Usually the tuberculous lymphadenitis appears painlessly, without constitutional upset, and the slowly progressive enlargement of the gland is discovered accidentally. Less often there is a sharp febrile reaction corresponding with the "fever of onset" in pulmonary primary infection, and the gland rapidly enlarges and becomes tender, simulating an acute pyococcal lymphadenitis.

The problem of tuberculous lymphadenitis is complex. If the gland breaks down the child will be left with a discharging lesion which will heal slowly, leaving an unsightly scar after a long period of dressing. We should therefore make every endeavour to diagnose the condition before abscess formation, while the glands are still firm and hard and the skin is unaffected. Here we are again helped by the use of the tuberculin test, by careful attention to the previous history, and by the clinical characteristics of the gland; but in many cases a period of observation will be required, for we must remember that some septic glands are not tender when first seen. The period of watching may be from one to three months, varying with the rate of glandular enlargement; but, once a firm diagnosis is made, my advice is that the regional lymph node should be removed by local dissection, leaving a neat scar which, in the cases we have so far done, does not give rise to further difficulties. Streptomycin is given for two to three days before operation and for about three weeks after. If the gland is not seen for some two years or so after its appearance and is partly calcified, the question of removal is sometimes more difficult, and I think there is greater justification for a conservative policy. Increasing size is the sign of activity, and usually close observation by doctor and parent will give enough warning to enable removal to be carried out before the skin is involved or the gland has become a soft abscess; yet sometimes, even after years of quiescence, the gland will suddenly enlarge and become a red abscess within a very few days.

Case 5. Primary Cervical Adenitis: Slowly Progressive Type

A boy aged 7 years, the fifth child in a family of six, of middle-class parents in good circumstances, was seen in January, 1951, with a history of repeated colds. There were no abnormal clinical signs and his tuberculin reaction was negative, but arrangements were made to see him again in three months.

On his second visit the situation had changed: in February he had had a febrile illness, during which a painless but persistent gland had appeared at the angle of the jaw on the left side. On examination the left tonsil was larger than the right, there was a firm painless enlargement of the tonsillar gland, and the tuberculin reaction was now positive. For another two months he was watched and the gland slowly became larger. He was finally admitted to hospital at the beginning of July, four months after the onset. Streptomycin was given for seven days and then a local dissection was made. The glands were caseous, but the wound healed well and has not given rise to any trouble since.

Streptomycin is also of great assistance in the cases of lymphadenitis with a sharp febrile response; it reduces the temperature and controls the periadenitis, so that a large gland mass will resolve into its component parts, making removal easier. Case 6 provides a good example.

Case 6. Primary Cervical Adenitis: Marked Febrile Reaction

A female infant aged 11 months, the second child in a good artisan family, had had no previous illnesses and no known contact with tuberculosis, but the family took milk neither tuberculin-tested nor pasteurized. Twenty-three days before coming to hospital she had seemed unduly listless and wanted to be nursed; two days later there was a slightly tender swelling at the angle of the jaw on the left. This was poulticed for five days, but increased rapidly in size. Since then the child had remained miserable and was difficult with her food; her general condition, however, was good. On examination her left tonsil was larger than the right, and below the left ear was a large mass of glands measuring 2 by 3 in. (5 by 7.5 cm.), smooth, firm, and slightly tender at the edges in front and behind. The overlying skin was not involved, but the gland was fixed to underlying muscle. The right tonsillar gland was palpable but small. The tuberculin reaction was positive and the child's temperature was 103° F. (39.4° C.).

Streptomycin was started immediately, being continued for 14 days. By then the left tonsil was much smaller, practically the same size as the right, and the gland mass had shrunk to 1½ by 2½ in. (3.8 by 6.4 cm.); the component glands could now be felt. Above all, there had been a great improvement in the child's general condition. Over the next week streptomycin was continued, but the glands remained the same size, so they were removed through a crease-line incision. The wound was soundly healed one month after streptomycin was started. Eighteen months later there had not been any further trouble.

Though streptomycin has been of great assistance in the treatment of glands at all stages, I think it is unlikely to be successful in dealing with a caseous mass, and should not be relied upon to effect a complete cure.

Primary Lesions on Skin

Finally, as I have already mentioned, there are occasional cases in which a primary complex is visible in the skin. Here the effect of chemotherapy can be very much more easily observed, particularly if the primary focus itself has been at the site of a cut or other trauma. I will quote only one example.

Case 7. Healing of a Primary Skin Complex with Streptomycin

A healthy boy aged 7 cut the inner part of his left heel by treading on a piece of glass while paddling eight weeks before admission to hospital. On his return home the wound, about 1 in. (2.5 cm.) long, was dressed by his grandmother. At first healing appeared to be satisfactory, but at the end of a week the grandmother must have been dissatisfied with his progress for she applied poultices. In another week a frank but painless ulcer had formed, and this persisted until his admission. One evening, about a month after his original injury, while bathing him, his mother found a lump in his left groin. As there was no pain little notice was taken until in another fortnight the mass enlarged and became soft and red. At this stage he was taken to the doctor and sent to hospital, where the inguinal abscess was incised and the ulcer on the foot was searched for a foreign body which might explain the failure to heal. A second incision was necessary a week later, and on this occasion tubercle bacilli were found in the pus from the inguinal adenitis. At this stage I was asked to see him, and found a granulating ulcer in the heel and an open incision in the groin. The tuberculin reaction was strongly positive, biopsy of the lesion on the foot showed tuberculous granulation tissue, and tubercle bacilli had already been recovered from the inguinal gland. Here again, therefore, was the primary focus associated with regional adenitis. Approximately nine weeks after the original trauma, streptomycin, 0.5 g. daily, was started, and within five weeks both the ulcer in the foot and the gland in the groin had completely healed. Since then the boy has remained well and there has been no recurrence.

There is no doubt that this healing was hastened by the use of streptomycin, for in untreated cases of primary skin tuberculosis healing has taken many months.

The visible effect of streptomycin in primary foci on the skin and in certain cases of primary tuberculous adenitis in the neck and abdomen again brings to mind the possible effect of antibiotics upon primary tuberculosis in the chest, and raises the question whether streptomycin and P.A.S. should not be used in all cases of "fever at onset" on the analogy that a febrile response to a primary infection is likely to be associated with a marked reaction in the regional glands. This is a very fair and open question, but I do not think that an affirmative answer can at present be given: certainly in practice we would not recommend streptomycin in cases with only a febrile reaction without signs of dissemination, unless the temperature remained elevated for more than four weeks.

Conclusion

In this paper I have indicated an approach to the management of a child with primary tuberculosis and the immediately local complications. I have demonstrated that we have not yet the data to answer some of

the most important questions—for example, the risk of meningitis at different ages—and that I do not think children with asymptomatic primary infection should be treated in sanatoria unless home circumstances are unfavourable, or by antibiotics except under very special circumstances. These children should nevertheless remain under regular supervision and a close watch be kept for signs of disseminated disease. Knowledge of the primary complex is, moreover, of great assistance in detecting the early case of tuberculous meningitis or miliary tuberculosis, in which the prognosis depends almost entirely upon the time interval between onset and the beginning of treatment.

The routine use of streptomycin and P.A.S. cannot be recommended, but in cases of prolonged fever of onset, or when the infant is infected in the first year and is febrile or losing weight, or in certain cases of tuberculous cervical lymphadenitis, these compounds are of very real value.

Finally, I would repeat my plea that, wherever home care is competent and conditions are good, children with primary tuberculosis who do require treatment should be kept at home or be allowed to go home as soon as possible after confirmation of the diagnosis in hospital. This applies particularly to the child under the age of 5 years, who should be admitted to a "long-stay" hospital only when no other course is possible. We must strike a careful balance between the chance of diminishing the risk of disseminated disease and improving the child's physical state and the chance of interfering with or distorting his emotional development by long separation from home and parents,

THE CHEMICAL ESTIMATION OF CORTISONE-LIKE HORMONES IN URINE

BY

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AND

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Now that the presence of adrenal cortical hormones in both blood and urine has been detected with certainty, the problem of quantitative assay of these hormones becomes a matter of increasing importance.

In blood the presence of 17-hydroxycorticosterone and also of corticosterone has been demonstrated by several workers (Reich, Nelson, and Zaffaroni, 1950; Pincus, Hechter, and Zaffaroni, 1951), but cortisone has not so far been detected in appreciable quantity. In urine both cortisone and 17-hydroxycorticosterone (compound F) have been identified (Burton, Zaffaroni, and Keutmann, 1951b) and actually isolated by Schneider (1950, 1952). They occur in urine in association with a number of other steroid compounds, most of which are probably devoid of biological activity.

The problem of assay of these hormones in biological fluids is made difficult by the small quantities which are involved, for present estimates indicate from 5–10 μg. per 100 ml. in blood and about the same concentration in urine.

The most direct estimation is achieved by use of a biological method, since the specificity of biological responses is high. Venning, Kazmin, and Bell (1946) have developed biological estimations based on the power of these hormones to encourage glycogen deposition in the liver of adrenalectomized mice. Similarly, Cope (1951) has developed, and Cope, Boysen, and McCrae (1951) have used, a method based on the ability of these hormones to depress the count of eosinophil cells in the blood of adrenalectomized mice. Although the latter method is appreciably less laborious than the former, yet both suffer from disadvantages inherent in their biological nature. They are technically difficult to perform, they require relatively large quantities of hormone-containing extract for assay, and they are inaccurate unless large numbers of animals are used for each assay. When accuracy is increased in this way still more labour is involved and still more material is needed. The reality of these deterrent factors is well indicated by the great scarcity of published work during the past six years on adrenal hormone assays in clinical material using the liver glycogen methods. The outstanding lead given by Venning (1945) has not been followed.

Although good approximations to the hormone content of urine extracts can be obtained with much less effort by the mouse-eosinophil technique, the need for a still simpler, and chemical, method of estimation remains. The observations reported here will, it is hoped, provide the basis for such a method. The difficulties to be overcome may be divided into three main groups: (*a*) quantitative extraction, (*b*) purification from interfering contaminants, and (*c*) quantitative estimation by a suitable chemical reaction. Each of these may be considered separately.

Quantitative Extraction

The state of the adrenal cortical hormones in urine is such that they cannot be extracted completely by the usual lipoid solvents such as chloroform. A preliminary hydrolysis is necessary to convert them into a chloroform-soluble form. The steroids probably exist in urine largely as sulphates and glucuronides (Cohen, 1951b). If the urine is acidified to *p*H 1 the former but not the latter are hydrolysed at room temperature. With stronger conditions of hydrolysis, such as warm acid, destruction of hydrolysed hormone may occur. Proper extraction of the hormone thus requires hydrolysis of the esters without destruction of the free hormone. Extensive studies have been made by several workers to determine optimum conditions of extraction for the formaldehydogenic steroids. The yield of these latter extracted with chloroform is increased 10 to 20 times if the urine is first hydrolysed with the enzyme β-glucuronidase (Cohen, 1951a; Daughaday, Farr, and Houghton, 1951). No studies have yet been reported on the effects of enzymatic hydrolysis on the recovery of biologically active hormones from urine, although their behaviour is likely to be similar.

Bayliss (1952), as a result of his studies on the extraction of the formaldehydogenic steroids from urine, has suggested an extraction procedure designed to recover the free hormone, the glucuronide, and the sulphate with the minimum of destruction by exposure to acid. This extraction involves three stages: (*a*) chloroform extraction after 48 hours' hydrolysis with β-glucuronidase, (*b*) immediate re-extraction after acidifying to *p*H 1, and (*c*) acid hydrolysis at *p*H 1 for 24 hours at room temperature and a third extraction with chloroform. In the belief that such a triple extraction represents the most complete extraction procedure at present available we have compared the yield of biologically active hormone obtained by its use with the

yield obtained by the more conventional single extraction with chloroform after 24 hours' acid hydrolysis at room temperature and *p*H 1.

Methods

Samples of urine from selected subjects were collected for three or four days. Each day's collection was halved. One-half was acidified to *p*H 1 and stood for 24 hours at room temperature before extraction four times with 15 volumes % of chloroform. This extract was prepared for bio-assay as described by Cope, Boysen, and McCrae (1951). The remaining half of each day's urine was adjusted to *p*H 4.5 with acetate buffer and treated with 50 units of β-glucuronidase per ml. for 48 hours at 37° C. The Bayliss (1952) type of triple extraction was then carried out, each extraction using three successive lots of 15 volumes % of chloroform. These extracts were combined and prepared for bio-assay in the usual manner. The final extracts from the four half-days were pooled. In this manner each day's urine could be extracted while fresh, bacterial action was minimized, and the separate extracts from acid hydrolysis and from the triple extraction procedure represented comparable samples of urine.

β-glucuronidase was prepared by the rapid method of Fishman (Talalay, Fishman, and Huggins, 1946) from rabbits' livers, spleens, and kidneys. The activity of the final product was 7,000 units per ml. when measured by the phenolphthalein-glucuronide method of Talalay, Fishman, and Huggins (1946). Bio-assay of the adrenal cortical hormones was performed by the method developed by Cope, Boysen, and McCrae (1951) using the eosinophil drop in adrenalectomized mice. Only three animals were used for each assay, since our mice were relatively insensitive and only the stronger extracts contained enough hormonal activity for a greater number of mice. To eliminate errors due to variations in individual mice the same three animals were invariably used for testing the glucuronidase triple extract as were used for the corresponding *p*H 1 extract from the same urine sample.

Results

Fourteen urines have been used for comparison of the yields by the two methods. The specimens have been chosen to cover the range from low to high content of active adrenal hormone. The results are shown in Table I, the samples being arranged in order of activity of the *p*H 1 extracts. The increase in yield by the triple-extraction method varied

TABLE I.—*Effect of Glucuronidase on Cortisone Extracted from Urine (μg. daily)*

Extract	*p*H 1 Hydrolysis (*a*)	Glucuronidase Triple Extraction (*b*)	% Rise in Yield on Glucuronidase Treatment $\frac{(b-a)}{a}\times 100$
1	0	0	—
2	50	190	280
3	50	207	315
4	120	158	30
5	140	250	78
6	170	185	8
7	180	315	75
8	192	270	40
9	195	240	23
10	240	520	117
11	300	480	60
12	320	600	87
13	342	696	104
14	360	636	76
		Mean percentage increase	99

from 8 to 315%. The mean increase for the series is 99%. Since the accuracy of assay by this method is low with the weaker extracts, the apparent greater percentage increases in yield from some of these may be fallacious. It may be concluded, however, that the triple extraction after glucuronidase increases the recovery of active adrenal hormone by an average of 100%, and that this applies to both weak and strong urines. It is possible that a further increase in yield may result from greater concentrations of β-glucuronidase, and this point is being investigated.

Purification from Contaminants

Among the reactions available for a chemical assay of adrenal cortical hormone the Porter–Silber reaction (1950) appears to hold the highest place for sensitivity and suitability. In this reaction a yellow colour with maximum absorption at 410 m.μ is produced when a solution containing the hormone is heated with phenylhydrazine in sulphuric acid solution. The colour is given by both cortisone and 17-hydroxycorticosterone, and its intensity is proportional to the concentration present over a considerable range. Nevertheless the reaction cannot be safely applied direct to the usual urine extracts because of the development of interfering pigments which also absorb light at 410 m.μ. Satisfactory reagent blanks cannot be prepared to compensate for this, because the pigments often give more colour with sulphuric acid alone than they do with the sulphuric acid and phenylhydrazine reagent. As a result erroneous figures are often given by the reaction on unpurified urine extracts, and apparent negative readings may be obtained on the less potent urines. This interference is due to substances other than the hormones themselves, and the colour of the hormones develops independently of the contaminating chromogens. Consequently the intensity of colour of the final solution, after allowing for reagent blanks, is the algebraic sum of the colour due to hormone with that due to contaminant. Because of this, the ability to detect quantitatively extra hormone added to a urine or urine extract is no proof that the method can reliably estimate the hormone content of the original urine or extract, since an unknown amount of contaminant colour is included in the latter.

Experience with two typical urine extracts may be used to make this point clear (Table II). The first extract, from a patient with Addison's disease, gave no detectable corti-

TABLE II.—*Recovery of Cortisone Added to Urine Extracts*

	Cortisone Added (μg.)	"Apparent Cortisone" Porter–Silber (μg.)	Recovery of Added Cortisone (μg.)
Extract A. Bio-assay: zero:			
3-hour aliquot	Nil	−10	—
" "	10	−1	9
" "	20	+11	21
" "	50	+42	52
Extract B. Bio-assay: 190 μg. daily			
1-hour aliquot	Nil	−11	—
" "	10	−1	10
" "	20	+10·5	21·5
" "	50	+40	51

sone activity in the mouse-eosinophil test. The Porter–Silber reaction applied direct to this extract gave a negative reading equivalent to −80 μg. a day. The second extract, from a patient with haemochromatosis, was deeply pigmented and had, according to mouse-eosinophil assay, a cortisone content of 190 μg. a day. In a one-hour aliquot of this extract the Porter–Silber reaction gave an apparent cortisone content of −11 μg., equivalent to −264 μg. a day. In both these extracts added cortisone, as acetate, could be quantitatively detected by the reaction in spite of the erroneous estimation on the original extracts themselves.

Carroll, McAlpine, and Noble (1951) have claimed that the Porter–Silber reaction can be used direct on urine extracts without further purification, yet they admit that negative values have often been obtained by them. They have not compared their results with analyses by an alternative method. For the reasons stated above, their ability to recover added cortisone is no proof of the reliability of the method for urine extracts, since no proper account is taken of the interfering chromogens. Although the Porter–Silber reaction can quantitatively detect cortisone added to urine

extracts in spite of the interfering chromogens, the estimation of the cortisone present in the original urine extract will be possible only if these interfering pigments can be removed or effectively neutralized. The problem is similar to that encountered in the chemical estimation of oestrogens.

We have attempted to remove those pigments by paper chromatography, using the system of Burton, Zaffaroni, and Keutmann (1951a). Both cortisone and the active hormone in urine extracts can readily be eluted from such paper chromatograms, using the toluene/propylene glycol system. Amounts may be recovered which are sufficient for assay by the mouse-eosinophil method. So far as the limited accuracy of this mouse method enables us to determine, the recovery by elution with methanol is almost complete. It was readily shown that all the biological activity of urine extracts remained in that part of the paper chromatogram representing a flow of less than $R_f=0.1$, and that an eluate of all the paper from $R_f=0.1$ to $R_f=1.0$ showed no detectable activity.

When chemical analysis of the eluate is being attempted it is preferable to use the benzene/formamide solvent system, because small traces of propylene glycol persisting in the eluate produce appreciable yellow colour at 410 m.μ, whereas traces of formamide produce no interfering colour. When cortisone is run for 24 hours in the benzene/formamide system and then subsequently eluted, the recovery varies between 75 and 95%. The mean of six trials, using amounts ranging from 35 to 300 μg. of cortisone, was 86% recovery.

When urine extracts are submitted to paper chromatography with the benzene/formamide system most, but not all, of the interfering pigment is fast-moving and can be removed. A small amount, however, has a slow rate of flow approximating to that of cortisone, and appears in the final methanol eluate containing the adrenal hormones. Considerable improvement is nevertheless obtained in this way, and the loss of quantitative accuracy entailed by the paper chromatography is more than counterbalanced by the advantages resulting from removal of the interfering pigment.

Quantitative Chemical Estimation

On urine extracts purified by such chromatography the Porter–Silber reaction seems to give a much more reliable index of the true adrenal hormone content. To show that this is so we have compared chemical analyses obtained in this way with biological assay of the same extracts by the mouse-eosinophil method. The degree of agreement between the two methods is such as to suggest that the differences in result still persisting are due mainly to the experimental errors of the two methods, which are considerable.

Methods

Urine extracts were prepared in the usual manner after either *p*H 1 hydrolysis at room temperature or after β-glucuronidase treatment with subsequent triple extraction as suggested by Bayliss (1952). Part of the extract was assayed by the mouse-eosinophil method, using three mice. Another part of the same extract, representing a known fraction in methanol solution, was applied to the starting line of paper chromatograms. At least 1 cm. width of paper was allowed for each one-hour aliquot of extract applied. The benzene/formamide system was used, and was allowed to run 24 hours at room temperature. The paper was then removed and dried free of formamide at about 50° C. overnight. The top 10 cm. containing all the active hormones was then cut out, divided into small pieces, and eluted with three successive lots of 20 ml. of methanol. Smaller volumes of methanol resulted in incomplete recovery. The 60-ml. eluate was evaporated to dryness *in vacuo* and was redissolved in exactly 2.5 ml. of methanol. One millilitre of this solution was used for analysis by the Porter–Silber reaction, and 1 ml. was used for the sulphuric acid blank. In some earlier experiments another area of paper from lower in the chromatogram was also eluted similarly to serve as a paper blank. Since the blank value from this was small, and as it was not strictly representative of the active area which still retained some non-specific pigment, these paper blanks were discontinued. A recovery of 85% was assumed and the appropriate correction was applied.

Results

The results obtained in 23 such direct comparisons are shown in Table III. With the exception of extract 6, estimates of cortisone content by both methods are of the same order of magnitude. In only two other extracts does the difference between the two estimates exceed 40%, and in 14 of the 23 the agreement is within 30%. The average difference (excluding extract 6) is +2%. The standard deviation from the mean is 27%. Since an error of at least 30% is to be anticipated in bio-assays carried out in this way, the agreement must be regarded as good.

TABLE III.—*Comparison of Chemical and Biological Assay*

Urine Extract No.	"Cortisone," μg. Daily		Percentage Deviation of Chemical from Bio-assay
	Bio-assay	Chromatography Chemical	
1	0	0	0
2	0	7	—
3	30	42	+40
4	146	106	−27
5	150	98	−35
6	158	(395*)	(+150*)
7	185	255	+38
8	190	224	+18
9	192	127	−34
10	240	188	−22
11	300	306	+2
12	300	203	−32
13	320	262	−18
14	320	353	+10
15	328	262	−20
16	342	344	0
17	360	330	−8
18	480	678	+41
19	520	474	−8
20	600	618	+3
21	636	659	+4
22	700	941	+34
23	1,116	1,706	+53
		Mean deviation % ..	+2
		Standard deviation from mean ..	27

* This anomalous result has been excluded in calculating the mean and S.D.

Discussion

The even scatter of the differences between the two methods of estimation suggests that they are due mainly to experimental errors, which are at present large in both methods. In urine extracts many other steroids occur, and some of these are probably present in the final methanol eluates from the paper chromatograms in greater quantity than the cortisone itself. Yet these inert steroids, of which tetrahydrocortisone is probably the most important, seem to produce no systematic error in the estimation. The amount of material producing yellow colour with the Porter–Silber reagent is apparently the same as that producing depression of eosinophil cells in the mouse. Only cortisone and compound F are known to cause such eosinophil depression in significant degree. It may be concluded that the Porter–Silber reaction can be satisfactorily applied to urine extracts purified by paper chromatography to give an approximate estimate of the content of cortisone-like hormones.

Schneider (1952) has been able to recover large amounts of a tetrahydrocortisone from urine extracts treated with β-glucuronidase. This and allied compounds must be expected to give a yellow colour with the Porter–Silber reagent, and these tetrahydrocortisone-like compounds, having a slow rate of flow in the chromatogram, will be present in the final eluates. When present in large amounts these compounds must be expected to interfere with the estimation of the cortisone and compound F in the chromatogram eluates. It is improbable that they are biologically active. We must presume from the agreement between bio-assay and chemical analysis that interference

from this cause has not been serious in our own urine extracts. But if greater specificity in analysis is needed then recourse must still be had to the biological methods of assay.

It seems likely that similar considerations will apply to the comparable method for the estimation of compound F in blood published by Nelson and Samuels (1952), whilst our own work was in progress, and that their method will be similarly capable of giving a reasonable approximation to the true compound F content of the blood extracts used.

Summary

The yield of cortisone-like hormone recoverable from human urine has been estimated after enzymatic hydrolysis with β-glucuronidase and chloroform extraction. It has been compared with the amount recovered after the more usual acid hydrolysis at room temperature.

The enzyme treatment increases the yield of cortisone-like hormone by from 8 to 315%, the mean increase being 99%.

The Porter–Silber colour reaction can detect quantitatively cortisone added to urine extracts, but often gives quite erroneous values for the cortisone-like hormone content of the extracts themselves.

Much of the interfering chromogen can be removed by paper chromatography.

On extracts purified by paper chromatography the Porter–Silber reaction can give estimates of cortisone-like hormone content which agree with the results of bio-assay of the same urine extracts.

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In a paper which he read to the New York Health Conference last year Dr. I. Galdston discussed some of the public health problems in that city. He mentioned that there was a corp of police in the New York subway to hand out summonses for carrying lighted cigarettes or cigars, though the staff was insufficient to provide adequate or decent toilet facilities. For that matter, he added, there were inadequate public toilet facilities through the whole city of New York, despite the ageing population. Again, in a city which stretches for more than 10 miles, there were "few facilities whereby the over-taxed heart, the aching bones, or the fatigued muscles might be given respite on a public bench or park seat."

17-KETOSTEROID EXCRETION IN GOUT

BY

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Wolfson *et al.* (1949) reported that urinary 17-ketosteroid (17-K.S.) excretion was low in gout. In a group of 11 gouty patients, representing all stages of the disease, the average excretion was 3 mg. per 24 hours, with a range of 0.67–6.6 mg. per 24 hours. They stated that biological evidence of androgen activity was normal in 9 of the 10 men in this group, and explained this seemingly anomalous finding by postulating the presence of an abnormal androgen in gout which, when metabolized, does not materially contribute to the urinary 17-K.S.

Later, Robinson *et al.* (1949) reported findings in which 26 determinations of 17-K.S. in 10 gouty patients gave values consistently lower than normal, both during attacks and in interval periods.

Material and Methods

Our findings were obtained from a study of 33 gouty patients (see Table).

Basic Data on 33 Gouty Patients, Showing Serum Urate and 17-ketosteroid Levels

Case	Sex	Age (Years)	Average Serum Urate*	17-K.S. (mg./ 24 hours)	Acute Gout Witnessed	Satisfactory Colchicine Response
			Recurring Acute Gouty Arthritis			
1	M	43	9·8 (5)	4·4		
2	M	53	6·6 (23)	7·4	+	+
3	F	68	6·7 (15)	5·4	+	+
4	M	55	5·6 (8)	10·9		
5	M	37	9·2 (21)	9·5	+	+
6	M	42	8·3 (18)	11·9	+	+
7	M	48	8·2 (6)	9·8	+	+
8	M	49	6·3 (5)	18·0		
9	M	57	5·1 (12)	8·3	+	+
10	M	36	7·8 (5)	16·4		
11	M	52	7·2 (7)	5·0		
12	M	69	7·5 (5)	6·7		
			Chronic Gouty Arthritis			
13	M	53	5·0 (22)	7·0	+	+
14	M	65	5·5 (19)	10·8	+	+
15	M	56	4·8 (17)	6·8	+	+
16	M	59	7·2 (8)	14·0	+	+
17	M	60	10·8 (16)	11·0	+	+
18	M	40	8·7 (11)	8·6		
19	M	70	6·8 (9)	10·0		+
20	M	64	9·9 (7)	11·9		
21	M	56	8·4 (13)	13·1	+	+
22	M	59	9·2 (3)	9·3	+	+
23	M	54	9·2 (12)	13·9	+	+
24	F	61	7·4 (11)	6·0	+	+
25	M	45	7·2 (4)	11·2	+	+
26	F	67	5·0 (9)	7·3	+	+
27	M	57	5·8 (9)	11·7		
28	M	62	9·1 (3)	12·3		
29	M	45	8·5 (3)	12·4	+	+
30	M	58	8·6 (3)	5·7	+	+
31	F	68	7·4 (20)	1·4	+	+
32	M	49	8·6 (14)	10·7	+	+
33	M	37	12·7 (13)	5·0	+	+
Average all patients		54·4	7·7	9·5		

* The numbers of serum urate estimations are given in parentheses.

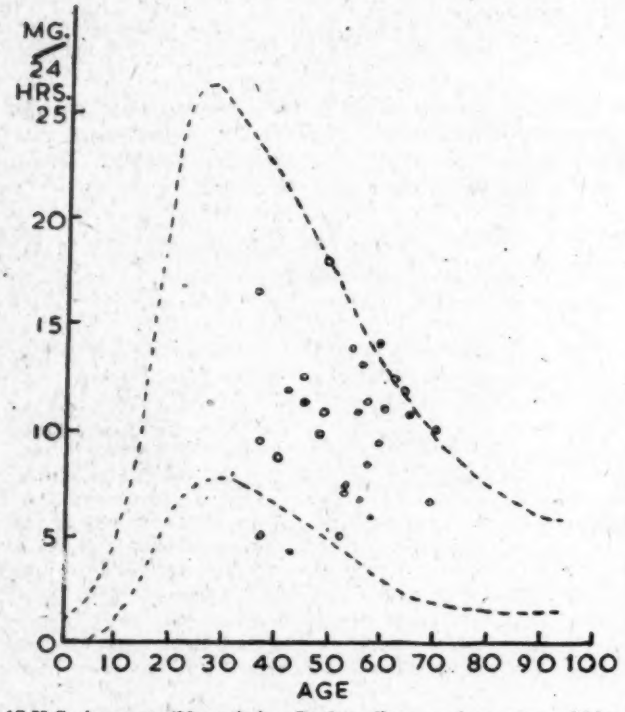
The neutral 17-K.S. values were obtained by a polarographic method (Barnett *et al.*, 1946a; Butt, 1950). Normal ranges for males are 10–20 mg. per 24 hours (age group 20–38 years), and for females 6–18 mg. per 24 hours (age

group 18–37 years) (Barnett *et al.*, 1946b ; Butt *et al.*, 1948). Wolfson *et al.* (1949) use a colorimetric method in which the normal ranges are stated to be 9–25 mg. per 24 hours for males and 7–12 mg. per 24 hours for females. These figures agree well with those of Hamburger (1948), who studied the variation of 17-K.S. excretion with age and sex in normal individuals. The urate estimations were performed colorimetrically by Brown's (1945) method.

Results

The excretion of 17-K.S. was measured in 29 male and 4 female patients suffering from gout. The average age of the subjects was 54.4 years, and the range of 17-K.S. was 1.4–18 mg. per 24 hours, with an average of 9.51 mg. per 24 hours.

The Graph shows the normal variation of 17-K.S. output (for males) with age (Hamburger, 1948). Normal outputs by our method all lie within this range : male cases in this series are plotted in the Graph. The outputs in the four female cases are within the corresponding female range.



17-K.S. in gout (29 males). Broken lines enclose area within which 97.1% of normal values lie (males) Hamburger (1948).

Discussion

Polarographic and colorimetric methods for estimation of 17-K.S. have been discussed by Barnett *et al.* (1946b) and Butt *et al.* (1951). Results obtained by polarography are comparable with those obtained by colorimetry if a colour correction is made. In some urine extracts, however, chromogenic substances are present which are not recognized by polarography, and in these cases the colorimetric method gives values considerably in excess of those found polarographically.

Wolfson *et al.* state that the non-ketonic chromogens are apparently disproportionately high in the urine of gouty patients, and that separation of the neutral ketonic material should be done with Girard reagent T. The polarographic method is particularly suitable here, as the estimation is done on the Girard derivative, and no colour correction is needed.

The 17-K.S. outputs obtained in this series are appreciably higher than those of Wolfson *et al.*, and fail to show any significant deviation from the normal range.

Summary

Urinary 17-K.S. outputs have been estimated in 33 gouty patients. The results show no significant deviation from normal values.

We have been unable to confirm that gout is characterized by a low 17-K.S. excretion, a finding first reported by Wolfson *et al.* (1949) and later by Robinson *et al.* (1949). Therefore we see no grounds for postulating the presence of an abnormal androgen in gout.

Our thanks are due to Professor A. P. Thomson, who was in charge of the clinical cases, and to the nursing staff, whose full co-operation is so essential in the collection of 24-hour specimens of urine.

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ACUTE ACETONE POISONING CAUSED BY SETTING FLUID FOR IMMOBILIZING CASTS

BY

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AND

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In recent years lightweight casts have been used for immobilization of limbs. These consist of glass and textile bandages which are set by means of a fluid consisting chiefly of acetone. They have the advantage of being easily penetrable by *x* rays, and it is therefore unnecessary to remove them when *x*-raying the immobilized limb. Because of their light weight they are often used for children.

It is not generally recognized that the setting fluid is a potential cause of serious poisoning. Indeed, this is not surprising, since we have found no adequate appraisal of the more severe toxic effects of acetone in the literature. Hamilton and Johnstone (1945), for example, write : "Acetone has an innocent history as far as its industrial use is concerned. Kobert said that it was almost inconceivable that poisoning could follow its use." We have had under our care a case of acetone poisoning following the application of a lightweight cast, and we feel that it is important to draw attention to the potential danger of this method of immobilization.

Case History

The patient, a 10-year-old boy, was being treated in a sanatorium for tuberculous arthritis of the right hip. His condition had improved while he had been immobilized on a plaster bed, and the orthopaedic surgeon in charge of the case decided to have a lightweight hip spica applied.

The cast was applied on January 11, 1952, by a male nurse in an extremely poorly ventilated theatre measuring 21 by 24 by 12 feet (6.4 by 7.3 by 3.7 metres). The room was very warm, being heated by means of metal plates in the walls.

After the occurrence of this case of acetone poisoning, temperatures taken in the room twice daily for one week ranged between 82 and 88° F. (27.8 and 31.1° C.). As the particular day was rather cold it is probable that the temperature of the room was in the region of 82° F. (27.8° C.).

The following details of the events while the patient was in the sanatorium, and before his admission to the Royal Victoria Infirmary, were obtained from the doctor in charge and from the male nurse.

The boy was taken into the theatre at 2.5 p.m. and was allowed to lie on a bed while the solution and bandages were being prepared. This took ten minutes. About 72 oz. (2 litres) of the setting fluid, which consisted of 90% acetone, 9% pentane, and 1% methyl salicylate, was used, the bowl containing the liquid standing near the foot of the patient's bed at a level of 3 in. (7.6 cm.) below it, and at a distance of about 6 feet (1.8 metres) from his head. The application of the cast, which reached from nipple level to the right ankle and included the left thigh, took 15 minutes. Following this the patient was allowed to lie on his bed, about 14 feet (4.3 metres) from his previous position, while a similar plaster was being applied to a second boy, using a further 50 oz. (1.4 litres) of the setting fluid. While his plaster was being applied the patient complained of the acetone fumes. After being in the room for one hour he was removed to a cool well-ventilated ward, and then seemed perfectly well, taking a normal tea at 4.45 p.m. Nothing abnormal was noted in his appearance or behaviour by the doctor while doing his ward round at 7 p.m.

Between 11 p.m. and midnight the night sister reported that the boy was restless and had a headache, and was complaining of his cast feeling tight across his abdomen. She examined it, and found that it was in fact quite loose.

At 3.15 a.m. the patient vomited purplish material (he had been having gentian violet, ½ gr. (32 mg.) t.i.d. for five days, for threadworms). At 4.45 a.m. persistent vomiting began, the vomitus still being stained with gentian violet, and in the meantime the patient became more restless. At 5 a.m. he collapsed, and his plaster was slit down the side at 5.30 a.m. By 7.30 a.m. the vomitus had become brownish in colour, and the boy was by now very pale and almost stuporous. His spontaneous speech was incoherent, but he could answer questions correctly. At 8 a.m. his blood pressure was 80/60. At 10 a.m. he began to complain of thirst and was given sips of water, which he would vomit each time. His cast was removed at 11 a.m. The inside of it was still wet and sticky and smelt of acetone, but the appearance of the patient's skin had not changed where the cast had been in contact.

He fell into a deep sleep at midday, waking periodically, asking for water, and then vomiting about ½ oz. (14 ml.) of brownish material each time after drinking it. At 1 p.m. his condition worsened again, and he expressed the fear that he was going to die. He was "deathly pale," but for the most part lay quietly. During the course of the morning arrangements had been made for his transfer to the Royal Victoria Infirmary, but he was not fit to travel until 2 p.m. He was admitted at 3.15 p.m. on January 12, 25 hours after the application of the cast.

On admission he was extremely ill and was apathetic, breathing deeply, rapidly, and irregularly, with occasional hiccups. His temperature was 97° F. (36.1° C.), his pulse rate 132, and his blood pressure 120/70. His face was pale with a slight malar flush, his ears were pink, and his extremities were warm. He was restless and had a dry mouth and an intense thirst. There was an extraordinarily strong odour of acetone in his breath, stronger than we had ever noted in cases of diabetic coma. Apart from limitation of movement of the right hip, a few small superficial pressure sores over the right calf, and extremely brisk tendon-jerks, no other abnormalities were detected on physical examination. After taking a drink he vomited 2 oz. (57 ml.) of brownish material, which on testing gave a prompt positive benzidine reaction. He passed 9 oz. (255 ml.) of urine in which acetone and diacetic acid were easily detected, and sugar (one plus) was detected with Benedict's reagent. His blood acetone level approximately 26 hours after the application of the cast was still 15 mg. per 100 ml.

A presumptive diagnosis of acetone poisoning was made and intravenous N/5 saline and 4.1% dextrose given. He remained very restless and continued to vomit blood-stained material. By 5 p.m: his respirations had slowed and he was having regularly recurring periods of apnoea lasting up to 25 seconds. The respirations, though similar to those of Cheyne–Stokes breathing, were more irregular and were interrupted occasionally by deep sighs. Vomiting ceased at 7.10 p.m., and by 8 p.m. it was obvious that his condition was improving. He was in a sleep, from which he could be roused by light touch.

By 11 p.m. his breathing, though still deep, had become regular again, at 28 a minute. He now began to notice people in the room, and volunteered the information that he felt better. His tongue had become moist and his colour more flushed. By the next morning, January 13, his condition had almost returned to normal, but the smell of acetone in his breath, though not pronounced, was still detectable. Acetone and diacetic acid were still present in his urine, but sugar was not found again. His tendon reflexes, though brisk, were less active than on the previous day. Intravenous fluids were discontinued at 8.45 p.m., 2,500 ml. of glucose-saline having been given.

By the fourth day he seemed quite normal, and we could not smell acetone in his breath or detect it, or diacetic acid in his urine.

The second boy, who had a similar cast applied, was 12 years of age. He slept normally that night, appearing perfectly well the next day until 7 p.m., 28½ hours after the application of the cast, when he vomited. He had no further symptoms.

Discussion

References to three similar cases have been found in the literature. Strong (1944) described the case of a 42-year-old physician who had had a body spica applied, using a setting solution of polymerized vinyl acetate, pyroxylin, boric acid, and acetone, followed by an acetone-containing lacquer. He vomited brownish material, and blood clots were aspirated from his stomach. He became comatose and, a mistaken diagnosis of diabetic coma having been made, was given several doses of insulin. He had transient glycosuria, and eventually recovered after an illness lasting several days and complicated by the diabetic treatment given.

Chatterton and Elliott (1946) describe the case of a girl of 10 years. Long leg casts were applied, the setting solution having the same constituents as that in Strong's case. An acetone-containing lacquer was also applied twice. After the second application of the lacquer the patient, who had been restless and having haematemeses, became semi-comatose, with Kussmaul's breathing. She recovered on the third day.

Fitzpatrick and Claire (1947) describe the case of a 21-months-old child with congenital dislocation of the hips. When a similar cast was applied under general anaesthesia recovery from the anaesthetic took approximately 20 hours, whereas on other occasions it occurred normally with the same anaesthetic and a conventional plaster cast.

The Table shows the main signs and symptoms with their times of onset, when stated, in cases of acetone poisoning by this mechanism.

These four cases of acetone poisoning, arising in a similar manner, present features in common which comprise a characteristic picture. After a latent interval of more than six hours the patient becomes restless, and shortly after begins to vomit with gradually increasing frequency. Before 24 hours have elapsed the vomitus contains altered blood, and by this time the patient is becoming stuporous, with Kussmaul's or periodic breathing. The degree of collapse may become profound, with the patient complaining of intense thirst. The smell of acetone in the breath may be striking, and acetone, diacetic acid, and sugar may be found

Author	Symptoms	Time of Onset after Application of Plaster
Strong (1944)..	Anorexia	6 hours
	Nausea and vomiting	10 ,,
	Vomiting brownish material	13 ,,
	Semi-consciousness and deep breathing of Kussmaul type	17 ,,
	Coffee-ground material and blood clots aspirated from stomach	35 ,,
	Following this, symptoms were confused by reason of diabetic treatment given	
Chatterton and Elliott (1946)	Fitfulness and restlessness; vomiting; haematemesis	1st day
	Kussmaul's breathing and semi-coma after application of an acetone lacquer	2nd ,,
	Weakness and listlessness followed by recovery	3rd ,,
Fitzpatrick and Claire (1947)	Emesis of dark brown material	7 hours
	Failure to recover from anaesthetic	20 ,,
Present authors	Patient complained of fumes during application; headache; restlessness; plaster felt tight across abdomen	9 hours
	Vomiting started	13 ,,
	Collapsed condition	15 ,,
	Vomited brownish material	17 ,,
	Excessive thirst	20 ,,
	Deep, rapid, irregular breathing; hiccup with periods of apnoea	25 ,,
	Proved haematemesis	26 ,,
	Vomiting ceased	29 ,,
	Irregular breathing ceased	32 ,,

in the urine. Recovery begins gradually late on the second day, and is eventually complete.

In considering this problem it is important to remember some of the physical properties of acetone. It is one of a group of volatile anaesthetics. It is heavier than air, so that concentrations of acetone at the level of the patient's face when he lies on a low bed are apt to be high. This may explain why the person applying the casts seems to suffer no ill effects. Acetone is freely miscible with water and therefore easily absorbed through the alveoli, so that high concentrations may be reached in the blood.

Under experimental conditions, probably on account of the relatively low blood concentrations achieved, toxic symptoms are mild. Koehler, Windsor, and Hill (1941) infused 10 g. of acetone in 200 ml. of saline over a period of two hours. The human subjects used for this experiment showed a slight fall in the systolic and diastolic blood pressures, and transient drowsiness was frequently observed. The average maximum blood acetone level in this experiment was 15 mg. per 100 ml. one hour after the injection had stopped, and nearly normal levels were obtained after 24 hours. It is therefore reasonable to assume that in our case, in which the blood acetone level 26 hours after the cast was applied was still 15 mg. per 100 ml., the maximum concentration at some stage after the application of the cast must have been much higher.

Under industrial conditions acetone may cause irritation of the mucous membranes of the eye and respiratory tract, headache, fainting, and, in much higher concentrations, narcosis. In higher concentrations it is more toxic for brief exposures than chloroform and is only slightly less toxic than benzene (Jacobs, 1949). Severe vomiting, haematemeses, and periodic breathing are not features of industrial or experimental acetone poisoning.

It is striking how in the cases of poisoning caused by the application of casts there has been a latent interval before the onset of symptoms, which does not seem to occur under industrial conditions. In the cases described by Strong and by Chatterton and Elliott, and in our own case, severe symptoms started at night. It is not uncommon for people to sleep with their heads under the bedclothes, where the concentration of acetone produced by vapour from the drying cast might be expected to be high. Our patient was accustomed to sleep like this, and this habit may at least partially explain the latent period. In a further effort to explain this, we considered the possibility of absorption of acetone through the skin. The only experimental work on this aspect appears to have been done by Cesàro and Pinerolo (1947), who found no evidence of acetone absorption through the skin in human subjects, but the exposure to acetone was not nearly as long or as intimate as in the conditions pertaining in the cases we are considering. Proof, therefore, that acetone *cannot* be absorbed through the skin under these conditions is lacking.

Owing to the physical conditions existing in the theatre in which this cast was applied, it is likely that the air near the patient's face contained a concentration of acetone of about 240 mg. per litre. If a normal respiratory rate and normal respiratory exchange are assumed, the amount of acetone inhaled in the 25 minutes might have been as much as 34 g. If a much smaller quantity of air were saturated with acetone vapours, as might occur under the bedclothes, the concentration could rise to 15 g. of acetone per litre. (Estimates made for us by Professor W. F. K. Wynne-Jones.) The recommended maximum allowable concentration for daily eight-hour exposures ranges from 0.5 to 5 mg. per litre of air under industrial conditions (Haggard *et al.*, 1944). The concentration of acetone in the theatre is therefore likely to have exceeded this by far, though the time of exposure was a good deal shorter. Nevertheless, it does indicate the need for careful consideration of the physical conditions under which the cast may be applied, and it is fair to state that the manufacturers warn that it is desirable to use their product in a well-ventilated room.

The possible toxic role of the pentane present in the setting fluid has been considered. It may have an anaesthetic effect, but as it is rapidly eliminated via the respiratory tract it has no cumulative effect, and it is therefore unlikely to have been an important factor.

In conclusion, we would urge that the following precautions be taken in using this method of application of immobilizing casts : (1) As little of the setting fluid as possible should be used. (2) Any lacquer used should not contain acetone. (3) This method should not be used for casts covering extensive areas of the body which require larger amounts of the setting fluid unless ventilation conditions are ideal. (4) During and after the application of the cast ventilation should be good and room temperatures should not be too high, as this would increase the amount of vaporization. (5) A blower or exhaustion fan would increase the rate of drying, but a shock-cradle would seem to be contraindicated in view of the possibility of a high concentration of acetone being reached under the bedclothes. (6) Patients and nurses should be warned of the possible ill effects of the subject's head being under the bedclothes.

Summary

A case of acetone poisoning, following its use in a setting fluid for an immobilizing cast, is described, and three similar cases in the literature are reviewed.

Certain precautionary measures are urged in the application of these casts. The clinical picture is characterized by a latent interval, followed by restlessness and vomiting, proceeding to haematemesis Progressive collapse occurs, with stupor and Kussmaul's or periodic breathing. Recovery, which begins gradually on the second day, is eventually complete..

We wish to thank Dr. J. H. Stobbs and Mr. J. G. Jameson, and the consultant staff of the Orthopaedic Hospital, for details of the case before admission to the Royal Victoria Infirmary, and Professor Sir James Spence and Dr. F. J. W. Miller for their interest and encouragement. We are also grateful to Professor W. F. K. Wynne-Jones, Department of Chemistry, King's College, for assistance with calculations of acetone concentrations.

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CHANGES IN THE DUODENAL CONTENT FOLLOWING CARBACHOL

BY

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Our knowledge of the effects of choline and its derivatives on the human pancreatic secretion is of comparatively recent date. This is partly because studies in the human subject require a special technique for the recovery of the content of the duodenum and partly because of the uncertain composition and unstable nature of the earlier preparations of the chemical mediator. Ägren and Lagerlöf (1936) overcame the first difficulty by resorting to a combined gastro-duodenal tube, which allowed the stomach and the duodenum to be drained simultaneously. Methacholine chloride *B.P.* (acetyl-β-methylcholine chloride, "mecholyl") was among the first of the synthetic analogues of acetylcholine to be investigated. It was shown by Comfort and Osterberg (1940) to affect the pancreas in a manner almost indistinguishable from that resulting from vagal stimulation. As is now well known, methacholine promotes an increase in the flow of secretion which, though less in quantity than that following humoral stimulation, is much richer in the three ferments; and the effect on the hydrogen-ion concentration is negligible. "Urecholine," the urethane of methylcholine chloride, is similar in its action (Kyle *et al.*, 1950).

It appears that these choline derivatives also exert an influence on the bile flow, as evidenced by an increase in the concentration of bilirubin and its total value per unit of time. This effect is usually detected with the naked eye. Comfort and Osterberg were inclined to ascribe these changes to contraction of the gall-bladder, but, as Kyle *et al.* pointed out, it may occur in those who have had their gall-bladder removed. There are grounds, therefore, for assuming that the cholines stimulate the flow of hepatic bile. Needless to say, much has been written about the nervous control of the bile flow.

The purpose of this investigation was to study the effects of carbachol (carbaminoylcholine chloride) on the duodenal contents, with particular reference to the changes in (1) volume and colour, (2) lipase concentration, and (3) the total lipase per unit of time.

Methods

Contamination of the duodenal juice was reduced to a minimum by the use of a modification of the gastro-duodenal tube, which was not procurable at the time this work was undertaken. Two Ryle's duodenal tubes were stuck together throughout their length by rubber solution. The bulbous extremity of the one intended for the stomach was then cut off and the cut end slit for a short distance to allow this part to be wrapped round the duodenal one about 10 cm. from the latter's extremity. Perforations were made in the gastric tube at a site which would ensure simultaneous emptying of the stomach and duodenum. The paired tubes were passed at 8 a.m., after a fast lasting approximately 10 hours. Ten healthy young adult male volunteers were studied. The technical procedure adopted for the withdrawal of the duodenal content followed that described by Diamond *et al.* (1939). After a basic flow had been established the duodenal fluid was decanted for testing every 10 minutes, the gastric fluid being discarded. Each subject received 0.25 mg. of carbachol intramuscularly. Four 10-minute fractions were taken off before and four after its administration. The lipase estimations were carried out by the method described by Cherry and Crandall (1932), and it was found convenient to dilute each sample to a strength of 1:10 with distilled water.

The Resting Duodenal Fluid

This is a clear yellow-to-amber-coloured fluid with an approximate *p*H of 8. The presence of turbidity or a fall in the *p*H values was taken to indicate contamination with gastric chyme. Suspected samples were discarded.

The *volume* recovered in the 10-minute periods varied from 0.5 to 15.2 ml., the average for all of the control samples withdrawn from the 10 subjects being 3.5 ml. This may seem a wide variation, but to the best of one's knowledge the fractions were composed of pancreatic juice, bile, and such secretions as came from the duodenal mucosa with the barest minimum of gastric juice.

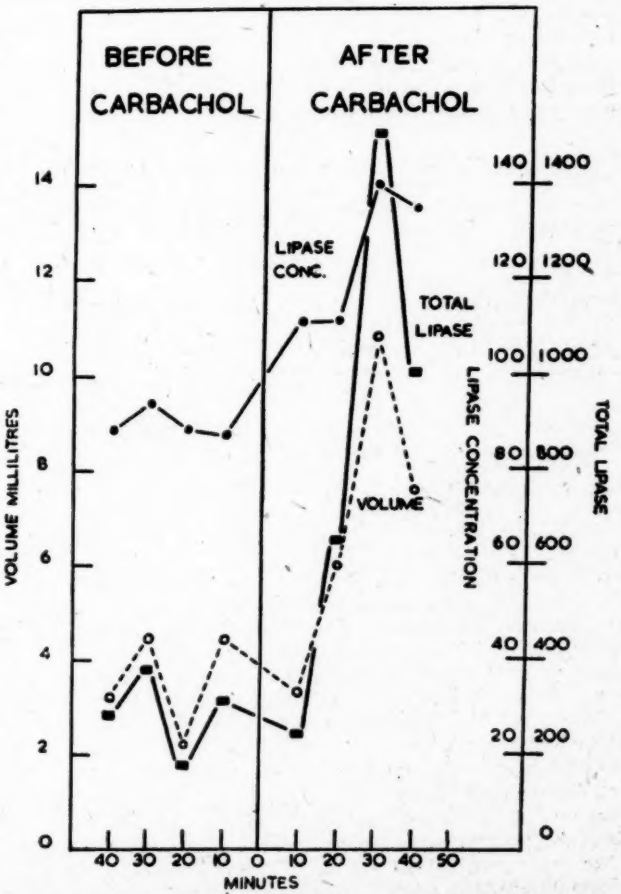
The *concentration of lipase* expressed in terms of millilitres of N/20 sodium hydroxide per ml. of duodenal fluid ranged from 46 to 136, the average being 91.7 ml.

The *total value for lipase* expressed in terms of millilitres of N/20 sodium hydroxide per total sample varied from 35 to 1,155.2, with an average of 303 ml.

The Effects of Carbachol

The *volume* of the duodenal content was increased in 7 of the 10 experiments. The change was most noticeable after 30 minutes.

In all except the first, a pronounced deepening of the normal *bile-staining* was observed within 10 minutes of the administration of the drug. The affected samples also became appreciably more viscous.



Composite graph showing average findings for volume of duodenal content and lipase concentration per 10-minute sample and lipase per total sample before and after carbachol.

The *concentration of lipase* was raised in all but two of the subjects. In three instances the values were modified within 10 minutes, but the response was not maximal until the third or fourth fractions.

The *total values for lipase* appeared to be raised in all except one, and again it was observed that the highest values were usually obtained 30 minutes after carbachol.

The averages for all the above findings are presented in the form of a composite graph.

Summary

"Pure" duodenal juice was obtained by applying continuous suction to two Ryle's tubes, one of which lay in the stomach, the other in the duodenum.

An intramuscular injection of 0.25 mg. of carbachol was given to 10 fasting young adult males. An increase in the volume of the duodenal content resulted in 7, an increase in the lipase concentration in 8, and an increase in the total value for lipase per unit of time in 9 of the subjects. On the whole these effects were most pronounced about 30 minutes after the giving of carbachol.

Evidence is presented that this drug also stimulates an increased flow of bile.

The findings indicate that carbachol excites the external pancreatic secretion in humans.

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Medical Memoranda

A Cauda Equina Lesion due to Spondylolisthesis

The following interesting case is rare enough to be placed on record.

Case Report

A man aged 52 had complained of partial incontinence of urine since October, 1945. In the previous January a road accident was the cause of a transient haematuria. Investigation at the former date revealed a distended bladder and a well-developed interureteric bar, which was divided through a cystotomy incision. This failed to improve the incontinence.

He was seen again in September, 1949, and in addition to his urinary difficulties his left foot felt useless and often caused him to fall. He had normal control over his bowels except when he had an enema or when he had diarrhoea and his bowel tended to prolapse.

On examination he was found to be a thin pale man dribbling urine and passing flatus without regard to social conventions. He had bilateral inguinal herniae and an incisional hernia below the umbilicus. No neurological abnormalities were found in the cranial nerves or arms. The optic disks were normal and the abdominal reflexes brisk. His left foot was seen to be plantar-flexed and inverted, and there was obvious wasting of the left calf and both buttocks. The knee-jerks were present, but the ankle-jerks were very weak even with reinforcement. Tone was normal and there was no clonus. Stimulation of the outer border of the soles brought no response. There were gross sensory changes. The areas supplied by L 1, 2, 3, 4, and 5 dermatomes had normal sensibility, but he had well-defined saddle anaesthesia over his lower buttocks and round the front of his anus and the posterior aspects of both thighs corresponding to S 1, 2, and 3. The anus was patulous. There was also alteration of the sensation on the lateral side of both soles, accounting for the absent plantar reflex. His joint and vibration sense was normal.

Detailed examination of his muscles revealed the following state of affairs (muscles found to have normal power are omitted from the Table):

Muscle	Main Segmental Innervation	Power (M.R.C. Classification)	
		Right	Left
Gluteus maximus	L 5 S 1	4	4
,, medius	L 4 and 5 S 1	4	5
Peroneus	L 5 S 1	3	3
Tibialis posterior	L 4	5	4
Gastrocnemius	S 2	5	3
Ext. hallucis longus	L 5	3	1
,, digitorum ,, ...	L 5	3	4
,, ,, brevis	S 1	0	0
Flex. ,, longus ..	S 2	5	2
,, hallucis ,, ...	S 2	5	2

Investigations.—His Wassermann reaction was negative. Radiological examination showed a gross localized osteoarthritis involving the third and fourth lumbar vertebrae and a second-degree spondylolisthesis (Prip Buus, 1943) at the lumbo-sacral articulation, with considerable osteoarthritic changes. These changes were present in the film taken in 1945, thus absolving the accident from blame. Cystoscopy: The bladder capacity was 1 pint (570 ml.), and the patient had the normal sensation of distension. There was fine trabeculation of the vesical wall, and the posterior urethra presented a funnel-shaped deformity, allowing extensive visualization of the prostatic urethra. No "bite" was felt when a large steel bougie was passed.

The patient was readmitted in October, 1949, with a transverse fracture of his left patella and again in March, 1951, with a similar fracture of his right patella, from a fall on each occasion. Both were sutured and united satisfactorily.

Comment

Organic nervous changes in spondylolisthesis are rare in spite of the extreme degree of subluxation which can occur. Burns (1931–2, 1934–5) and other authors deny that it ever happens. Heinrich and Krupp (1938) suggest that such changes are seen only in pure traumatic lesions such as fracture or total dislocation of the vertebra. They emphasize that riding-breeches anaesthesia and sphincter disturbances are but rarely seen. Lane (1893) reported a case in which he operated, but this was probably due to a prolapsed intervertebral disk. Friberg (1939) found sensory changes in 8 out of 302 cases, and Meyerding (1931, 1938) in less than 2% of his 583 patients. Of the 27 patients reported by Prip Buus, three had sensory changes and only one a cauda equina lesion.

The mechanism of the lesion is not as obvious as it first appears. By extradural myelography Prip Buus has shown that the posterior longitudinal ligament becomes detached from the posterior surface of the slipping vertebral body (usually the fifth lumbar), and that there is no narrowing of the spinal canal. If anything, the antero-posterior diameter is increased. Even in Stage IV, when the fifth lumbar vertebra is in front of the first sacral and its lower border sunk below the level of the upper border of S 1 (spondyloptosis), he considers that the size of the canal is still adequate to accommodate the cauda equina. Furthermore, the intervertebral foramen is situated close to the vertebral body and accompanies its related body during the forward shift. Thus the nerve is not impressed directly and, if anything, becomes more relaxed. This I have confirmed by direct measurement on the skeleton.

A coincidental prolapsed intervertebral disk has been incriminated for the neurological disturbance, but in Prip Buus's case of cauda equina lesion no such disk was demonstrated on myelography. Prip Buus concludes that the nervous dysfunction is attributable to a chronic irritative arachnoiditis or to a chronic inflammation of the extradural tissue.

In the present case the bilateral fractured patellae cannot be directly related to the cauda equina lesion, as no part of the reflex quadriceps arc was found defective. His fractures were undoubtedly due to faulty balance caused by muscular weakness below the knees.

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Chronic Intermittent Juvenile Jaundice

Meulengracht (1947) published a review of 35 cases of chronic intermittent juvenile jaundice, and a further case was described by Parkes Weber (1948). This condition must be considered in the differential diagnosis of mild jaundice and is probably more common than the number of published cases suggest, for three cases have recently been seen in this hospital. The familial incidence in two of these and the different modes of presentation may be features of interest. The biochemical and haematological investigations were repeated in each case at different times, but only one set of typical results for each subject is given in the Table.

Test	Method and Normal Range	Case 1a	Case 2a	Case 2b	Case 2c	Case 3
Blood:						
Haemoglobin (g./100 ml.)	Haldane	13·3	16·2	15·9	18·2	14·8
Haematocrit (mm./100 mm.)		40·0	48·0	—	52·0	44·5
Reticulocytes		0·3%	<1%	0·8%	0·4%	0·4%
Van den Bergh (direct)		Weak, pos.	Pos.	Pos.	—	Weak, pos.
Total bilirubin (mg./100 ml.)	Evelyn and Malloy. <0·75	2·0	4·1	2·7	4·0	1·8
Phosphatase (units)	King and Armstrong. 3·7–13·1	5·9	5·7	7·1	—	9·6
Thymol turbidity (units)	Maclagan. <4	3	1	1	—	1
Kunkel's turbidity (units)	<4	2	2	4	—	1
Plasma proteins (total) (g./100 ml.)	Micro-Kjeldahl. 5·6–8·5	6·25	—	—	—	6·07
Albumin (g./100 ml.)	3·4–6·7	4·70	—	—	—	4·25
Globulin (g./100 ml.)	1·2–2·9	1·55	—	—	—	1·82
Red-cell fragility (% saline)	Commenced lysis	0·46	0·46	0·46	"Normal"	0·44
	100% lysis	0·28	0·28	0·28	—	0·28
Direct Coombs test		Neg.	—	—	—	Neg.
Faeces:						
Stercobilinogen (mg./24 hr.)	Schwartz, Sborov, and Watson. 40–280	125	—	—	—	69
Urine:						
Urobilinogen	Ehrlich	0	Tr.	Tr.	—	0
Urobilin	Schlesinger	0	"	"	—	0
Bilirubin	Fouchet	0	+	+++	—	0
Bile salts	Hay	0	0	0	—	0

CASE REPORT

Case 1a.—A woman aged 20 complained of nausea and lassitude. On examination her conjunctivae were slightly yellow, but on physical examination she was otherwise normal, neither her liver nor spleen being palpable. Recurrent attacks of jaundice had occurred in the past, but these had spontaneously improved as did this episode. There was no significant change in the physical and laboratory findings during a further attack some six months later. *Case 1b:* Her brother, aged 24, had experienced two similar attacks of jaundice in addition to prolonged neonatal physiological jaundice. When seen, he was normal physically and his blood and urine showed no abnormality on laboratory testing. Opportunity has not occurred for laboratory investigations to be made during an icteric phase.

Case 2a.—A man aged 29 suffered attacks of jaundice with pain in the right hypochondrium at the ages of 7 and 17. During a similar attack, when aged 23, he had a cholecystectomy at another hospital, when "20 to 30 small brown currant-like stones" were removed. Despite this his jaundice persisted, but he was free from pain for five years. He was referred for investigation because of another attack which had been present for about two months. On examination he was slightly jaundiced though free from any other abnormalities apart from his operation scar. *Case 2b:* His brother, aged 27, was first noticed to be jaundiced when aged 12 and has been so since. Otherwise he is normal and suffers no inconvenience. *Case 2c:* The third brother, seen elsewhere, has very slight jaundice, said to have been present from birth. No other members of this family are known to have shown similar symptoms.

Case 3.—A man aged 25 was noticed to have an icteric serum during routine bleeding for antibody investigations. He had been perceptibly jaundiced for as long as he could remember, but had no other symptoms. His condition was unchanged over a period of more than a year. There was no relevant family history.

COMMENT

Each case presented in a different guise. Case 1a was investigated because of recurrent attacks of jaundice accompanied by nausea and lassitude, and the possibility of a subacute hepatitis of insidious onset as described by Kelsall, Stewart, and Witts (1947) was considered. The normal laboratory findings, with the exception of raised serum bilirubin, in conjunction with the long history and the suggestive history of her brother confirmed the present diagnosis. Case 2a had already undergone cholecystectomy and when first seen the possibility of familial haemolytic jaundice was considered. Once more the haematological findings excluded this, the biochemical findings were equivocal and could be interpreted as those of a hepatitis, but again the long history, the absence of abnormalities in turbidity tests and the alkaline-phosphatase tests in conjunction with the family history led to the diagnosis of chronic intermittent juvenile jaundice. The appearance of bilirubin in the urine of Case 2a and one of his brothers is presumably related to a higher plasma concentration of bilirubin in these cases, though Vickers (1950) emphasized that bilirubin cannot be considered a threshold substance. The third case was asymptomatic, and a slightly raised total serum-bilirubin was the only laboratory abnormality.

Our thanks are due to Dr. R. S. Bruce Pearson and Professor C. H. Gray for advice and criticism, and to Dr. A. Gilpin and Dr. W. M. Davidson for permission to publish one of the cases and the haematology results respectively.

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Reviews

MEDICINE AND THE AGED

Cowdry's Problems of Ageing: Biological and Medical Aspects. 3rd edition, edited by Albert I. Lansing, Ph.D. (Pp. 1,061; 215 figures. £5 14s.) London: Baillière, Tindall and Cox. 1952.

Problems of Ageing. Transactions of the Fourteenth Conference, September 7–8, 1951. Edited by Nathan W. Shock. (Pp. 138. $3.) New York: Josiah Macy, jun., Foundation. 1952.

The substantial increase, both relative and absolute, in the numbers of the older members of the population in most civilized countries of recent years has resulted in more attention being given to the medical and social problems of the elderly than ever before. Considerable interest has been shown in the treatment of elderly patients, particularly in those suffering from the degenerative diseases which seem to be the particular perquisite of old age. At the same time much work is being carried out in an attempt to answer the two questions: What is ageing? and, Why does it occur? Dr. Lansing, in bringing out the third edition of Cowdry's *Problems of Ageing*, has assembled 47 co-workers who discuss fully and comprehensively both sides of the problems. That we know many of the details of the ageing process is clear from these papers, but it is also clear that our knowledge consists in a number of isolated facts which need eventually to fall into their correct place, as pieces in a jig-saw puzzle. There is much more work to be done before the puzzle can be completed. Certain facts disclosed here are startling—as, for example, Clive McCay's studies on the effect of diet upon ageing. He shows how retarding the normal rate of growth in rats by a cutting down of the number of calories in the diet gives them a longer life than is seen in rats allowed to mature normally.

On the clinical side the contributors emphasize the fact that disease among the elderly is but a branch of disease in general, and therefore is as susceptible to treatment as other diseases. This belief has spread widely during the past few years, and it is now being realized that the aged should be given as good a chance of recovering from their illnesses, or at least to overcome the disabilities resulting from these illnesses, as younger people. Elman, in discussing the surgical problems of the aged, points out how older ideas on the failure of ageing tissues to heal have been shown to be false. Dangers of infection have been reduced by the use of antibiotics and the sulphonamides, while, partly from experience gained during the last war, considerable knowledge is now available on the relief of that cardiovascular stress which once had so serious an effect on the prognosis of elderly patients submitted to major surgical operations. He has some particularly sound comments on the benefits to be obtained from the early ambulation of elderly patients. Improvements in anaesthesia have greatly widened the field of surgical interference in elderly patients, and Evelyn Apogi summarizes this new work well. Rusk, whose work at the Bellvue Hospital, New York, has been so remarkably successful, contributes a lucid and encouraging chapter on the rehabilitation of the aged. Here he maintains the valuable principle that the work of the doctor has not ended until the patient "is retrained to live and work with what he has left."

Apart from the few examples quoted, this book is full of valuable information, which is well presented. Unfortunately, its price—and its weight—may well militate against as wide a use as it deserves.

The report of the 14th Conference of the Macy Foundation is interesting. Lively, rather informal discussions were held over a wide field, covering biology, economics, welfare, and medical services for elderly people. The book gives much useful material on methods in the U.S.A. and in some European countries, and this will repay reading by any interested person. The report of the meetings is given in full; while this has certain advantages, it tends at times to confuse the reader.

AMULREE.

THE DELINQUENT CHILD

The Earliest Stages of Delinquency. By H. Edelston, M.B., D.P.M. (Pp. 200. 10s. 6d.) Edinburgh and London: E. and S. Livingstone. 1952.

The increase in the figures for juvenile delinquency has of late aroused a growing concern in the minds of parents, teachers, and education officials, and induced many local education authorities to establish child guidance centres. Dr. Edelston's aim is to explain the principles adopted in such centres, and to emphasize the need for studying "the patient's total personality in all its aspects, physical, intellectual, and emotional." His account falls into three parts. The first describes the origin and nature of child guidance and summarizes the methods used. Child guidance, he claims, is the "logical outcome of the findings of analytic psychotherapy"; and in his opinion the "new psychiatric approach" offers the best hope for dealing with the problem. In the second part he discusses a series of illustrative cases and their treatment, with special reference to "severe characterological disorders." The final chapters review the chief "findings and remedies," and end by stressing what he calls the "modern tendency"—namely, dealing with the potential delinquent at the earliest possible age. Here he might with advantage have mentioned the inferences drawn from statistical analyses of numerous after-histories, recently published in America — namely, that, "except for pathological cases, success seems most frequently achieved when the young delinquent is regarded, not merely as a patient in need of psychotherapy or a pupil in need of intellectual instruction, but as a growing individual whose character needs to be trained or re-formed."

Since during school years the effective handling of potential delinquents must lie largely in the hands of teachers, it is perhaps disappointing that so little is said about the ways in which they can co-operate. Older teachers, brought up on Sully's *Handbook*, may be tempted to reply that "child study" and "child guidance" were phrases and ideas popularized by James Sully long before the introduction of "analytic psychotherapy," and that Sully was the first to show the importance of investigating every aspect of the case, environmental as well as psychological, and of beginning if possible during the pre-school stage. However, the very fact that both educationists and psychiatrists, though approaching the problem from different points of view, have eventually converged on almost identical conclusions should be doubly convincing.

Dr. Edelston's account is both clear and eclectic; and his book may be safely recommended to medical practitioners and others who may be looking for a concise but comprehensive introduction to the subject.

CYRIL BURT.

CULDOSCOPY

Culdoscopy: A New Technic in Gynecologic and Obstetric Diagnosis. By Albert Decker, M.D., D.O.G., F.A.C.S. Foreword by Richard W. TeLinde, M.D. (Pp. 142; illustrated. 17s. 6d.) Philadelphia and London: W. B. Saunders Co. 1952.

Culdoscopy is the name given by Dr. Decker and Dr. Cherry in 1944 to the procedure of inspecting the female genital organs by means of a specially designed endoscope passed through the posterior vaginal fornix into the cul-de-sac (pouch of Douglas). Dr. Decker not only designed the modern culdoscope but also showed that, if the operation is carried out with the patient in the knee–chest position, the dangers and difficulties encountered by earlier explorers of the pouch of Douglas are avoided. In this monograph he describes and illustrates the technique in detail, and gives the results of his unrivalled experience. The use of culdo-

scopy in the diagnosis of ectopic pregnancy, pelvic endometriosis, and the causes of infertility receive special attention. Other subjects include the use of the vaginal approach for the induction of pneumoperitoneum, gynaecography, high-pressure therapeutic tubal insufflation controlled by culdoscopy, and endoscopic photography.

Dr. Decker has successfully avoided the pioneer's temptation to make extravagant claims and to overstate his case. In regard to culdoscopy in the diagnosis of ectopic pregnancy, for example, he writes, "The procedure should be reserved for cases in which the history and physical findings are atypical and the diagnosis has not been disclosed by other means."

Many gynaecologists are inclined to dismiss culdoscopy as unnecessary and unwarranted, taking the view that any case in which it might be indicated is one in which it is better to carry out laparotomy to have a "proper look." Dr. Decker's monograph, however, certainly leaves the reader with the impression that culdoscopy may have something to offer, both as a diagnostic aid and as an instrument for research into tubal and ovarian function.

T. N. A. JEFFCOATE.

SURVEY OF THE HORMONES

Hormones: A Survey of their Properties and Uses. Published by direction of the Council of the Pharmaceutical Society of Great Britain. (Pp. 220; 34 figures. 35s.) London: The Pharmaceutical Press. 1951.

The council of the Pharmaceutical Society is to be congratulated on this excellent book, the modernity and scope of which is a complete refutation of any antiquated conceptions of the limitations of pharmacy. The first-rate contributions of invited scientists such as H. E. Dale, C. W. Emmens, D. H. Hey, and T. D. Whittet are equalled by those of anonymous members of the council, and valuable clinical contributions are made by P. M. F. Bishop, J. F. Wilkinson, and P. R. Evans.

Initial chapters on history and physiology judiciously select sign-posts from an overwhelming mass of literature. Such is the concentration on steroid chemistry to-day that a chapter on the forgotten non-steroid hormones is very welcome. The recent work of Gross, Pitt-Rivers, and Trotter on 3:5:3′-L-tri-iodothyronin will no doubt be included in the next edition.

The section on the chemistry of the steroid hormones is for the expert, but is so set out that the clinician can visualize how small variations in the basic cyclopentenophenanthrene nucleus produce a variety of gonadal and adrenal hormones; and something of the magic of the synthesis of testosterone, dehydro*iso*androsterone, oestradiol, and corticosterone will not escape him during his intellectual application to an inevitably concentrated but lucid and inspiring text. The chapter on standardization is readable and informative. The clinical section is relatively short, but it provides more basic and logical clinical endocrinology in 36 pages than the reviewer has often reviewed in 360. This is a book that no doctor or student should miss acquiring and keeping.

S. LEONARD SIMPSON.

TEXTBOOK OF RADIODIAGNOSIS

Lehrbuch der Röntgendiagnostik. By H. R. Schinz and others. 5th edition. Part 7: Innere Organe. (Pp. 452; 515 figures. M. 89.) Stuttgart: Georg Thieme. 1952.

This volume is the seventh section of a great textbook of radiodiagnosis and it maintains the high standard of its predecessors. The first part is on the arteries, including the aorta and the arteries of the heart itself, and on the various diseases by which they may be affected. The heart itself was discussed in a previous volume. This is followed by a section of great interest on the part played by heredity in disease of the heart and lungs. It is of a most original character and is illustrated by tables which must have involved extensive research.

The remainder and the bulk of the volume is devoted to the upper intestinal tract and is really superb. The amount which can be learnt from radiology of the anatomy and physiology of the digestive system will be a revelation to many, as will be the light which this throws on the pathological conditions to which the bulk of the section is devoted. It is impossible to discuss it in detail, but perhaps one might refer to the double-contrast radiographs of the stomach by which abnormal characters of the mucous membrane are clearly displayed.

The whole volume is a monument of industry and of superb technique. It is profusely illustrated and will amply repay study by those who do not know a word of German. But those who are so fortunate as to be able to read it will find a mine of information, presented with the greatest clarity, the obvious result of vast experience and most careful work. It is a volume in every way worthy of the greatest traditions of the schools from which it comes.

HENRY SOUTTAR.

THE TONSILS

Tonsil and Allied Problems. By Roy H. Parkinson, M.D., F.A.C.S. (Pp. 432; 250 figures. £4 10s.) New York and London: The Macmillan Co. 1951.

In view of the frequency of operations on the tonsil (between one-third and one-seventh of all operations performed on town dwellers) the author decided there was need for a book on the organ, and he has certainly spared no pains to produce a really comprehensive work. Of the eighteen chapters, the first eleven are devoted to gross and microscopical anatomy, embryology, and physiology. Then follow four chapters on the diseases, common and rare. Some of the statements scarcely agree with opinion in Britain—for instance, that hyperkeratosis may be mistaken for diphtheria; no mention is made of the white spots on the lingual tonsil as a diagnostic sign, nor is its spontaneous disappearance stressed. Again, none of the common manifestations of syphilis of the tonsil are primary; even in V.D. clinics tonsillar chancre is rare.

The author fully discusses glossophargyngeal neuralgia arising from a tonsillar cause; he injects cobra venom into the nerve through the soft palate, using a special gold needle. If this does not cure, he advises intracranial section of the ninth nerve, and describes the operation with illustrations. Few throat specialists in Britain would perform this operation. Later he discusses the tonsil as a focus of infection, and follows this with a long description, more suitable to a textbook of medicine, of the various treatments of rheumatoid arthritis. The section on tumours of the tonsil and nasopharynx calls for comment; papilloma is said to become malignant occasionally and therefore should be removed on principle; treatment of fibroma of the nasopharynx consists in the removal of the growth with a snare when its size will permit—surely dangerous advice.

The last three chapters are excellent and are evidently founded on the author's wide experience. In them he discusses the indications for tonsillectomy, its performance, and the complications that may follow operation. One may not agree entirely with the list of indications, but generally they are sound. From the many detailed illustrations of the various stages of the operation even the inexperienced should be able to remove tonsils. For the unusual complication of haemorrhage after removal of adenoids packing the nasopharynx is advised and fully illustrated. The final figure shows the surgeon's whole hand in the mouth pushing the plug up into the nasopharynx and must be there by accident. The book is profusely illustrated, here and there in colour. There are 436 references, all American except for a few English ones on the anatomy and surgical anatomy. The author modestly states that he has not attempted to consult every article pertaining to the subject; nevertheless he has produced what may be described as an encyclopaedia on the tonsil.

W. M. MOLLISON.

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THE WORLD MEDICAL ASSOCIATION

In a recent broadcast Miss Barbara Ward[1] said that "if we are going to give the individual citizen his full scope in modern society, we have got to go beyond the nation and beyond the State, and look forward to various forms of international co-operation, because if we do not do that, we shall not even be able to give him the good life inside his own national society." This very remarkable statement would seem to suggest that the State or the nation needs some supranational supervision if the individual is to be able to keep his head above the collectivist waters of his own nation. A paradox indeed! Yet experience shows that a truth is there, concealed within the paradox. As was said at the general assembly of the World Medical Association at Athens last month, if the W.M.A. did not exist it would be necessary to invent it, and, partly perhaps, because of the reason given by Miss Ward.

Since its foundation in 1947 the W.M.A. has held six general assemblies in different parts of the world. Forty-three national medical associations make up its membership. The highly successful meeting in Stockholm last year under the presidency of Dr. Dag Knutson showed that the W.M.A. was now establishing itself as an international organization whose views had to be taken into account by other, and often governmental, international bodies. During the past year it has made its voice heard in the World Health Organization and the International Labour Office, in particular in the proposals of the latter for minimum standards of social security.[2] The W.M.A. has intervened in this matter because of its concern to preserve the freedom of the individual doctor in medical services provided under schemes of social security, thus vindicating the truth of Miss Ward's reason for international co-operation. During the past year, too, the W.M.A. has made much headway in its preparations for the World Conference on Medical Education[3] to be held in London in August, 1953. This is a theme always with us and to-day presents a new challenge to the medical profession the world over. It is said in the current issue of the *World Medical Association Bulletin*[4]: "Now, then, is the time to take stock. Medicine, still an art, has become so much more a science. Has medical education, in its conception and methods, kept pace with the advances of medical sciences?" Among other bodies, the W.M.A. has the active co-operation of the World Health Organization in next year's Conference, the outcome of which will in time affect the well-being of the future doctor, and so of the persons who come under his care in health and disease.

From Stockholm to Athens, where this year's general assembly was held, was a move from one extremity of Europe to the other, a move from a secure well-ordered community to one slowly but surely recovering from war and civil strife, a recovery that owes so much to Marshall aid. The enthusiasm with which our Greek colleagues, under the new president of the W.M.A., Dr. George Krimpas, received the delegates to the assembly showed, as in Stockholm, that the doctors of the nation had a real appreciation of what the W.M.A. meant and what it could do for them in the improvement and maintenance of professional standards and in the safeguarding of professional interests. Once again lively interest was shown in the debate on social security, and Dr. E. A. Gregg and Dr. Rowland Hill, on behalf of Britain, went far to correct misconceptions still widely prevalent about the working of the National Health Service. Dr. Gregg expressed his belief that the N.H.S. would ultimately be "knocked into such shape as would be acceptable to the majority of reasonable people." Another matter that stirred the interest of the assembly was a proposal that there should be set up an international association of the medical press. Two separate moves in this direction appear to be coming from France and from Italy; no information about these was available on the agenda and the assembly wisely referred the matter to the next meeting of the W.M.A. Council. A conference of medical editors is now a regular feature of the annual meeting of the W.M.A., and interest in this grows each year. At this papers are read and discussed, and a new feature at Athens was a "round-table discussion" of certain chosen editorial problems. It is difficult to see what editors would gain by adherence to still another international body.

The W.M.A. has come to stay. There can be no doubt of that. But it still leans too heavily on the generous financial support given it by the United States Committee. More active financial support must in time come from the various national medical associations, which represent in all some 700,000 practising doctors. If each of these were to give two shillings (or their equivalent) a year to the W.M.A. its

[1] *The Listener*, October 23, 1952, p. 671.
[2] *British Medical Journal*, August 2, 1952, p. 271.
[3] Ibid., August 30, 1952, p. 480.
[4] *W.M.A. Bulletin*, 1952, 4, 241.

financial position would be stable. Many tasks lie ahead for the W.M.A. in its efforts on behalf of the individual doctor. But it needs the interest and support of individual doctors if it is to accomplish these and help, to paraphrase Miss Ward's words, "to give the doctor the good life inside his own national society."

PROFESSIONS IN PERIL

That service to the community transcends service to the individual, and is somehow ethically superior, has been a prevalent belief in Britain since the war. As the members of the various professions have been increasingly brought into State employment, propagandists have often chosen to answer their misgivings by exclaiming on the services that will now be available to all instead of to only a privileged few. In this drift to collectivism there is a growing danger that the individual and individual values will be submerged in what may be mistakenly thought to be the common good. Britain's silent revolution, Lewis and Maude argue in a new book,[1] also seriously imperils the future of the professions themselves.

They have some difficulty in defining what a profession is, so numerous are the claimants to that status now and so ambiguous the position of occupations once undeniably professional. But they distinguish especially what they call the "moral behaviour" governing relations between practitioner and client or patient. They see in this something more than pride in doing the job well; certainly it includes a high sense of duty towards client or employer. But a doctor employed by the State may be in a quandary if the State's demands run counter to those of his patient, and they do not improve on Dr. T. F. Fox's conclusion[2] that "a professional man cannot admit to having an employer in the full sense . . . he does his work not under orders but as he thinks fit." A doctor would withdraw from a case, or ought to do so, if he is unable to act freely in accordance with his professional conscience—that is, as his professional judgment guides him, irrespective of the demands of State or patient.

Examining the traditions, notably those of medicine, on which the all-important practitioner-client relationship has been built up to become the keystone of professional conduct, Lewis and Maude contend that only with great difficulty will genuinely professional standards, as distinct from mere technical efficiency, be maintained when opportunities for private practice almost disappear. They conceive of private practice as the origin, preserver, and indispensable condition of the ethical relationship peculiar to professional practice, and write: "It is the free, rather than the controlled, professions which set the standard and justify professional prestige, just as it is the private practitioner, rather than the salaried man, who sets the individual moral standard—or, by letting it down, only proves its validity." Though they have in mind, besides medicine, professions whose members are much more directly employed by the State than doctors are, their warning is a timely one to our profession to consider seriously how best its great traditions of independent service to the individual can be preserved. And many will agree with the implication of their book that private medical practice, having diminished to an extent that endangers professional freedom, ought by some means to be resuscitated before a generation has grown up unaware of the vitality and sense of personal obligation it brings to the practice of medicine.

If a profession such as medicine whose members are almost wholly State-employed is to continue to serve patients with traditional fidelity and to receive their trust, it must play a large part in governing its own affairs. The curare-like effect of ceaseless injections from Whitehall is unlikely in the end to leave the doctor–patient relationship unscathed. Nor is it only the central administration that Lewis and Maude blame. They have some pertinent things to say about the increasing number of lay hospital administrators, whose institute "has manœuvred to become almost as much a closed profession as medicine," and question whether men of the necessary quality of character and personality are obtaining administrative posts. There is the risk that the training will turn out persons adept at agendamanship but lacking the understanding of human problems necessary if the right kind of encouragement and leadership is to be given. But meanwhile the Treasury "shows no sign whatever that it thinks it could trust the medical profession and its auxiliaries to handle . . . large sums of public money honestly," and its bureaucratic control too often destroys or diverts energies from the main task before medical men. Apart from the barbed-wire entanglement presented by its accounting methods, a more insidious danger is that standards quite other than professional are apt to be imposed on professional work. Much greater local responsibility on professional men in deciding how money from a Treasury block grant should be spent is what Lewis and Maude advocate, in common with many other critics—with a side-glance at the relative

[1] *Professional People*. By Roy Lewis and Angus Maude, M.P. London: Phoenix House, Ltd., 1952.
[2] *Lancet*, 1951, 2, 171.
[3] *The Duchess of Malfi*, Act 1, Sc. 1.
[4] *Memorandum and Articles of Association and By-laws of the B.M.A.*
[5] *British Medical Journal Supplement*, 1952, 2, 83.
[6] *British Medical Journal*, 1952, 1, 615.

independence of the universities. Until the two partners of the marriage between profession and Treasury have something like separate banking accounts, the relationship will be an unhealthy one, and the union "more properly be said," in the words of one of Webster's characters, "to be executed than celebrated."[3]

The function of professional associations has inevitably changed in response to the new relationships between their members and the State—and not by any means for the better, these writers argue. They fear that, if present trends continue, "the importance of the traditional professional association itself may . . . tend to diminish in the eyes of the younger generation in comparison with that of the bargaining association; or professional functions will come to be thought less important than bargaining functions where these are combined in one organization." The B.M.A. has this dual role of concern with both professional and bargaining functions, and is by this fact subject to the risk to which Lewis and Maude draw attention. The B.M.A.'s first object is "to promote the medical and allied sciences, and to maintain the honour and interests of the medical profession."[4] It is perhaps inevitable that the "interests" have too obviously appeared in recent years to be financial. For example, the triumph of the hard "bargaining" that resulted in the Danckwerts award may obscure in some minds the real significance of a voluntary association of professional men and women. Bargaining there has to be. We are by no means at the end of it. But this must be seen as but a part, and not even the most important part, of the activities of a professional organization. A statement by the World Medical Association[5] appended to its ninth principle has some relevance here. "The cultural and ethical standards of a civilized society depend for their maintenance and promotion principally upon the integrity and example of the learned professions. . . . There is a grave danger that social security schemes, however idealistically conceived, will progressively diminish the cohesive moral and cultural force emanating from the corporate life of the learned professions. The fundamental fallacy of the planners of social security schemes is the ignoring of this force, coupled with a tendency to regard practising doctors merely as technicians employing certain technical skills." Now more than ever is it the task of professional organizations to keep alive and renewed all that the term "learned profession" stands for, and the multifarious activities of the B.M.A. show its awareness of the importance of this. As Mr. Roy Lewis suggested in an article published in this *Journal*,[6] professional leadership should be "consciously professional."

THE SUPPLY OF INSULIN

"Monopoly" is a word which carries sometimes discreditable, even sinister, implications. According to one quotation from the Oxford Dictionary, a monopoly is "an unlawful method of traffic when one or more persons make themselves sole masters of any commodity . . . and design to enhance its price." Nevertheless, there are monopolies which work out to the public advantage, which protect instead of exploiting the public. One such is described in a *Report on the Supply of Insulin*, recently presented to Parliament by the Monopolies and Restrictive Practices Commission.[1] Almost the whole of the insulin supplied in the United Kingdom is produced by four manufacturers—namely, Allen and Hanburys Ltd., the British Drug Houses Ltd. (these two manufacturing it jointly as the A.B. Partnership), Boots Pure Drug Co., Ltd., and Burroughs Wellcome and Co. These concerns are organized loosely as "British Insulin Manufacturers" (B.I.M.). Their total sales in 1950 amounted to 3,000 million units, of the value of over one and a quarter million pounds, and more than half this quantity was supplied to the home market, that is to say, to the retail chemists and the hospitals. The number of diabetic patients in the United Kingdom is 200,000, of whom probably 60–70% are receiving insulin, mainly through the National Health Service.

Although the name "insulin" was coined as long ago as 1912 to indicate the antidiabetic principle secreted by the pancreas, it was not until ten years later that the process of extracting ox pancreas and applying it for the treatment of diabetes mellitus was worked out by Banting and his colleagues in Canada. It was felt to be an immediate duty to prevent the exploitation of the public in the case of a remedy of such world-wide importance, and to secure some control over the commercialized product. Patents were applied for in several countries, and these, when issued, were assigned to the Governors of the University of Toronto. Three British patents were granted, but before the first of these was taken out the University of Toronto assigned to the Medical Research Council the prospective rights under it in the United Kingdom. The report notes that the Medical Research Council, "though averse in principle to any proposal for the patenting of medical preparations," decided to accept the University's offer and to control insulin manufacture by licensing under the British patent. The production of insulin was begun in eight hospital laboratories, and clinical trials were instituted. The Council intimated that it pro-

[1] Published by H.M. Stationery Office, price 1s. 6d.

posed to limit closely the number of licences to manufacture and supply the material. British-made insulin was first marketed in April, 1923: the retail price was then 25s. for a standard pack, consisting of 5 ml. (20 units per ml.) of the unmodified product. The price came down to 6s. 8d. within a year, and since then it has continued to fall until in 1950 it stood at 1s. 5½d. In the interval the Therapeutic Substances Act, 1925, provided for the fixing of official standards for insulin among other substances, and the Pharmacy and Poisons Act, 1933, laid down certain requirements affecting insulin. The four manufacturing concerns work closely with each other and with the officers of the National Institute for Medical Research. The method of insulin manufacture now used by each of them is essentially the same, and includes some secret processes which together are called the "B.I.M. know-how." Their technical experience is pooled, patents obtained by one firm are made freely available to the others, and co-operative purchasing of ox pancreas has steadily improved the quality of the material available.

The Monopolies and Restrictive Practices Commission, under the chairmanship of Sir Archibald Carter, was asked by the Board of Trade to investigate and report on the supply of all forms and preparations of insulin. Accordingly it sought the views of the Ministry of Health and four other Government departments, the National Institute for Medical Research, the pharmaceutical organizations, and, among other bodies and persons, sixteen selected hospitals with diabetic clinics. The opinions obtained are uniformly commendatory. The Ministry of Health and the National Institute believe that the quality of British insulin is unsurpassed, that the members of the B.I.M. show great public spirit in all that concerns the interests of diabetics, and that the degree of co-operation between insulin manufacturers is incomparably greater than that between manufacturers of any other drug. The Ministry approves generally of the collaboration, with the single qualification that in its view "competition on price is desirable." Although the retail prices are the same for the products of each of the concerns, there are no sanctions against the lowering of the price by any one of them, and the understanding between them that no one manufacturer should lower his price without first informing the others is regarded by the Commission as not unreasonable. In fact, the information given to the Commission suggests that insulin prices in the United Kingdom are now the lowest in the world, with the possible exception of those charged in Scandinavian countries. The Ministry of Food, the director of the Department of Biological Standardization of the National Institute for Medical Research, the chairman of the Diabetic Association (Dr. R. D. Lawrence), and a number of other authorities gave their unqualified commendation, and the report of the Commission concludes with the remark that the arrangements now made by the manufacturers individually and collectively for the supply of insulin operate, and may be expected to operate, in the public interest. It is not often that a monopoly is praised; that the monopolists in this instance should be so closely associated with the service of medicine is an additional ground for satisfaction.

GAMMA GLOBULIN IN PROPHYLAXIS OF POLIOMYELITIS

A leading article in this *Journal* a few weeks ago on immunization against poliomyelitis[1] referred to the possible use of gamma globulin in these words: "Hammon's[2] suggestion that passive or combined passive–active immunization should be given a field trial during an epidemic needs careful consideration. It may provide a reasonably simple method of protection, but, as with any other method, would need careful planning and a large amount of blood." A preliminary report[3-5] has now come from the United States on the evaluation of gamma globulin as a prophylactic agent in poliomyelitis, and it is encouraging.

The principal aim of the project was to determine whether gamma globulin given in adequate dosage before infection would protect against paralytic disease. There was reasonable evidence from the laboratory that gamma globulin afforded protection against subsequent peripheral inoculation of virus,[6 7] of which the most virulent is Brünhilde. But would it work in man? Furthermore, would passive immunity prevent inapparent infection from taking place? In the first of three papers Drs. Hammon, Coriell, and Stokes[3] report the planning and results of the pilot test carried out in Utah in 1951. The trial was based on the random selection of children (aged 2–8) from an area in which poliomyelitis was likely to become epidemic. Alternate cases were to receive gamma globulin, the others a control injection of an inert substance (1.5% gelatin) with physical properties similar to those of the globulin preparation. American Red Cross gamma globulin was chosen, since it was known to contain neutralizing antibody to all three types of virus.[8] The nature of the injection solution was known only to the distributors. It so happened that the number of cases of paralytic poliomyelitis in the inoculated group (5,767) was too small for critical evaluation. However, valuable experience had been gained, the public confidence secured, and no harmful effects were observed. In accordance with the experience in Utah various modifications in planning

[1] *British Medical Journal*, 1952, **2**, 551.
[2] *Pediatrics*, 1950, **6**, 696.
[3] *J. Amer. med. Ass.*, 1952, **150**, 739.
[4] Ibid., 1952, **150**, 750.
[5] Ibid., 1952, **150**, 757.
[6] Bodian, D., *Fed. Proc.*, 1952, **11**, 462.
[7] —— *Amer. J. Hyg.*, 1951, **54**, 132.
[8] —— *Proc. Soc. exp. Biol., N.Y.*, 1949, **72**, 259.

were made, and last July a further 33,137 children (aged 1–11) in Texas, Iowa, and Nebraska were inoculated.[4] In the final paper Drs. Hammon, Coriell, Klimt, and Stokes[5] present a preliminary analysis of 90 cases of paralytic poliomyelitis in 54,772 children inoculated up to the beginning of October, 1952. Of these, 26 had received gamma globulin and 64 gelatin. Protection appeared to last about five weeks, and some evidence was obtained that the disease, though not prevented, was modified when gamma globulin was given within a week of the onset.

These encouraging findings afford valuable evidence that gamma globulin will protect against paralytic disease in man. But is the protection purely passive? That is the crux of the problem. The usefulness of this procedure will depend on whether inapparent infection has taken place. The results of the tests now being carried out to establish this vital fact will be awaited with the greatest interest. The possibilities opened up by this work are great indeed. We would do well in Britain to consider without delay how they can be used to full advantage. There seems little doubt that an even larger supply of blood products will be needed in the future.

MODE OF ACTION OF PENICILLIN

Penicillin poses a fascinating problem to the biochemist and bacteriologist, for its action is highly selective, and it is one of the most highly active toxic substances known against those bacterial species which are sensitive to it. There is not yet any clear or simple answer to the question how it works. Like other antibiotics useful as chemotherapeutic agents, penicillin has no action on the respiration, fermentation, or catabolic amino-acid metabolism of sensitive organisms so long as they are not multiplying. If cells are allowed to grow in the presence of the drug, then a series of alterations in the metabolism and composition of the resulting cells occur. Mitchell and Moyle[1] found an impairment of nucleic-acid synthesis after addition of penicillin to the medium in which *Staphylococcus aureus* was growing; Gale and Taylor[2] showed that cells progressively lose the ability to take up glutamic acid from the medium; while Gros, Beljanski, and Macheboeuf[3] found that the cells lose the ability to dissimilate guanylic acid under these conditions. Still later come progressive loss of respiratory activity and eventual lysis of the dying cells. These various effects all take place during growth and reorganization of the cells and may well be a consequence of some more fundamental inhibition. Hotchkiss[4] pointed out that such a primary effect should be demonstrable in non-growing cells, and he was able to show a disorganization of protein synthesis in washed suspensions of *Staph. aureus*, since addition of penicillin resulted in the formation of extracellular peptide-like materials instead of cellular protein as in the control experiments without penicillin. However, these results have not been repeated in other strains and under other conditions and may also be secondary effects. Other workers[3 5] have described inhibition of nucleic-acid breakdown by penicillin but have had to use concentrations many times greater than those required to prevent growth. A further indication of interference with nucleic-acid metabolism has been obtained by Park,[6] who finds that, after adding penicillin to the growth medium, a series of new nucleotide-like substances accumulate within *Staph. aureus* cells. He has identified these substances as derivatives of uridine-5′-pyrophosphate, an amino-sugar, and certain amino-acids.

It seems clear that penicillin acts somewhere in the cell's synthetic systems concerned with the production of proteins and nucleic acids. It has long been suspected, from somewhat indirect evidence, that nucleic acids are concerned in the organization of amino-acids within protein molecules, and perhaps the action of penicillin is concerned with a disorganization of such biosynthetic interactions of nucleic acids and proteins. This matter has been discussed at the recent International Congress for Biochemistry, when Gale[7] showed that the addition of nucleic-acid precursors to suspensions of *Staph. aureus* greatly increased their ability to synthesize protein, but that this effect was abolished by penicillin. High concentrations of the antibiotic were again necessary to effect a complete inhibition of protein synthesis, but it was pointed out that complete inhibition of the synthesis of all the proteins in the cell is probably not necessary to prevent growth: it is more likely that inhibition of a single specific protein is all that is needed. Evidence was produced showing that penicillin prevents the "turnover" of a specific portion of the protein within the cells, and that this effect is obtained at bacteriostatic levels of the drug. Complete interpretation of this effect must await further knowledge of the biochemistry of these synthetic processes. The many indications of the action of penicillin now available all suggest an interference at the protein–nucleic-acid level, and perhaps investigations of this nature will help to elucidate the mechanisms of protein synthesis.

A further important contribution was made by Hotchkiss at the Congress.[8] He showed that penicillin resistance can be transferred in pneumococci in a manner similar to that demonstrated some years ago by Avery and co-workers[9] for the transformation of capsular polysaccharides in these organisms. If sensitive pneumococci are cultivated in a medium to which has been added an extract of penicillin-resistant pneumococci, a proportion of the resulting organisms are penicillin-resistant and continue so on sub-cultivation. The active material or "transforming factor" appears to be a desoxyribonucleic acid, and Hotchkiss has shown that the penicillin-resistance factor is different from, and independent of, the capsular-polysaccharide factor. Penicillin resistance is therefore determined by the desoxyribonucleic acid composition of the cell and can be transferred, with the result that sensitive cells can be made resistant without ever being in contact with penicillin.

[1] *J. gen. Microbiol.*, 1951, **5**, 421.
[2] Ibid., 1947, **1**, 314.
[3] *Bull. Soc. Chim. biol.* (*Paris*), 1951, **33**, 1696.
[4] *J. exp. Med.*, 1950, **91**, 351.
[5] Krampitz, L. O., and Werkman, C. H., *Arch. Biochem.*, 1947, **12**, 57.
[6] *J. biol. Chem.*, 1952, **194**, 877, 885, 897.
[7] *Mode d'Action des Antibiotiques*, 2nd International Congress of Biochemistry, 1952, p. 5.
[8] Ibid., p. 40.
[9] *J. exp. Med.*, 1944, **79**, 137.

REFRESHER COURSE FOR GENERAL PRACTITIONERS

THE DIAGNOSIS OF SMALLPOX.—I

BY

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It is not too wide of the mark to suggest that a large part of the difficulty in the correct diagnosis of smallpox is created by the facility with which the disease can be portrayed in a written description. These canonical descriptions of the "typical" case of smallpox and the "typical" case of chicken-pox, which are enshrined in every textbook, encourage the belief that such clear-cut issues are usually encountered. The plain fact is that, in its typical form, the diagnosis of smallpox presents little difficulty; when the disease occurs in a person who has been vaccinated some time previously, however, almost every rule can be broken, so that a correct clinical diagnosis may be extremely difficult.

The roots of clinical experience of any disease require constant nourishment from a day-to-day acquaintance with it; the relative freedom of Great Britain from smallpox in recent years makes such conditions impossible. It is fortunate, therefore, that the virologist has now achieved both precision and rapidity in his examination of suspected material. While it will be obvious that the clinician should exercise reasonable discretion in the demands he makes upon the already overburdened resources of the virus laboratory, it is essential to make the important point that there is now no room for the confident assertion of a dogmatic clinical opinion in doubtful cases; the final answer must rest with the laboratory.

Pathogenesis of Smallpox

An understanding of the behaviour or natural course of an infectious disease is an essential prelude to its management. In smallpox such understanding must depend very largely on an analogy with another infection. The studies of Fenner on the pathogenesis of ectromelia, an infectious disease of mice, have supplied a useful working hypothesis which may be applied to smallpox. Such work as has been done on the disease itself tends to confirm the accuracy of the analogy. It would seem likely that reception of the virus is followed by a transient viraemia (Fig. 1). This

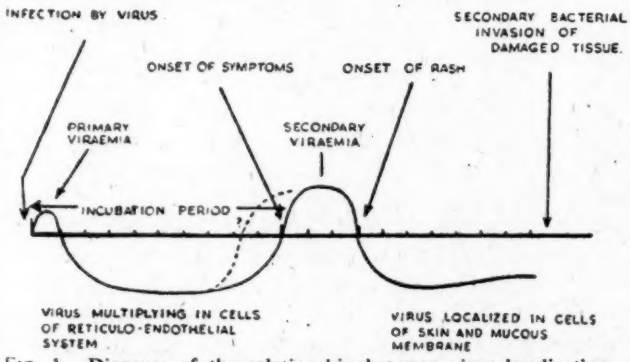
INFECTION BY VIRUS
SECONDARY BACTERIAL INVASION OF DAMAGED TISSUE.
ONSET OF SYMPTOMS
ONSET OF RASH
PRIMARY VIRAEMIA
SECONDARY VIRAEMIA
INCUBATION PERIOD
VIRUS MULTIPLYING IN CELLS OF RETICULO-ENDOTHELIAL SYSTEM
VIRUS LOCALIZED IN CELLS OF SKIN AND MUCOUS MEMBRANE

FIG. 1.—Diagram of the relationship between virus localization and clinical symptoms in smallpox.

primary viraemia inaugurates the incubation period during which time the virus is presumed to multiply in the reticulo-endothelial tissues. At the end of the incubation period the virus bursts into the blood stream (*secondary viraemia*), to be disseminated through it to all tissues of the body. Parasitizing of cells and multiplication of the virus now takes place—most obviously in the skin and mucous membranes, but probably also in many other tissues. The period of secondary viraemia is probably of short duration; further multiplication of virus occurs locally in and around the infected cells.

Although such an account may tend to oversimplify the matter, it forms a useful picture of the pattern of the disease and helps us to understand certain points which require emphasis:

(1) Vaccination after exposure may fail to prevent the disease. Once the primary viraemia has occurred prevention of the disease will depend upon a race between the multiplication of virus within the reticulo-endothelial system and the elaboration of virus-neutralizing antibodies as a result of the stimulus of vaccination. Early vaccination may, but will not always, prevent the disease: late vaccination, as Ricketts has said, "will merely add to the patient's troubles."

(2) The occurrence of the secondary viraemia in a susceptible individual sets in motion a sequence of events which it seems impossible at present to modify—namely, the localization and multiplication of virus in tissue cells. This will produce the typical skin lesions, and when these are numerous, as in the unvaccinated, a profound toxaemia due to a combination of local virus proliferation and tissue destruction will be a natural sequel. When the rash is profuse, too, the interference with normal skin function may well play a decisive part in enhancing the already grave intoxication.

(3) This local tissue destruction will permit the entry of a new phase into the disease—namely, secondary bacterial contamination. Added to the load which the patient already bears, this may well prove the final insult. Although, in theory, it is now possible to deal with this aspect of infection, it will be obvious that the contribution of chemotherapy is limited. For in the severe unmodified attack the effects produced by virus proliferation, tissue destruction, and interference with skin function will be the main deciding factors—effects which will be uninfluenced by antibiotics. Chemotherapy is more likely to be successful in limiting the worst features of the modified disease and in mitigating the disfiguration which, even in such cases, can result from unrestrained sepsis.

Prodromal Illness

The onset of smallpox is usually fairly abrupt. The temperature rises sharply—102 to 105° F. (38.9 to 40.6° C.)—and there are all the signs and symptoms of a generalized toxaemia, of which severe frontal headache, backache, nausea, and vomiting are the most constant features. Slight shivering or even rigors are common, particularly in adults, and the clinical picture is very suggestive of severe influenza. Conjunctival injection, suffused facies, dry coated tongue, marked prostration, and even violent delirium may all be noted in the most severe cases and heighten the resemblance to influenza possibly with lung involvement. This initial toxaemia, which usually lasts two to three days, is almost invariable in smallpox. Although its duration bears little relation to the subsequent illness or to the previous vaccinal state, the severity of the symptoms is usually related to the subsequent severity of the disease. By contrast, such a form of onset is unusual in chicken-pox, in which the first manifestation of the disease is often the appearance of the eruption. Although there are, of course, exceptions (and, particularly in adults, it should be remembered that chicken-pox can be a severe disease), it may be taken as a useful general rule to regard with great suspicion any case of apparent chicken-pox in which the rash has been preceded by a period of toxaemia.

During this prodromal period rashes, sometimes of fleeting duration, may be observed. The worst omen attaches to the purpuric form in which haemorrhage occurs into skin and mucous membranes and from mouth, bowel, or vagina. This, purpura variolosa, is usually seen in unvaccinated persons and is invariably fatal. Erythematous, macular, or pleomorphic rashes are occasionally seen. As a general rule the significance of these rashes is not so serious, although a vivid, intense, almost erysipelatous erythema is sometimes seen accompanying the purpuric form.

The Rash

The smallpox eruption, then, makes its appearance some 48 to 60 hours after the onset of a prodromal toxic illness. As a rule, coincident with its appearance the temperature drops sometimes to normal and the patient feels temporarily relieved of some of his toxic symptoms. The first lesions are usually observed on the forehead or the wrists, but, dependent upon the degree of modification, further lesions rapidly appear during the following 24 to 36 hours. It will be most convenient to trace the development of the rash through its sequence of changes. The description of the rash can be considered under three headings: first, the individual element; secondly, the distribution of the rash; and, thirdly, the variations that may be encountered.

The Individual Element

Macule to Papule.—Although the initial spots are macular and not raised above the normal skin, they rapidly become papular. The papules are usually rather small, of a dusky red colour, rounded, hard, and well defined. To the finger they feel in or almost under the skin and "shotty." The base of the papule is soon surrounded by a ring of erythema. The papules continue to increase in numbers, sometimes for as long as 48 hours; by this time some of the earlier lesions may begin to show vesication at the summit.

Vesiculation.—Although the change from papule to vesicle occurs more or less synchronously, in the more profuse rashes, as has already been indicated, the early papules have often begun to vesicate before the papular rash is complete, so that there may be as much as 24 hours between vesiculation in the upper and lower extremities. The vesicle is regular in shape with a rounded base, rather larger than the papule—about ¼ in. (0.6 cm.) in diameter—but, like it, giving the sense of lying deeply in the skin. Rather flat-topped to begin with, as the vesicle matures a central umbilication will often be observed, while later still the lesion may be dome-shaped. As development of the most profuse rashes takes place, neighbouring lesions tend to coalesce, particularly on the face, the forearms, and the back of the trunk. The skin feels hot, and in the most severe cases is very tender to the touch. Oedema is often a noteworthy feature, particularly obvious in the face.

FIG. 2.—The "seeds" of the late stage of smallpox.

Pustulation.—The contents of the vesicle are at first fairly clear, but over a period of two to three days a gradual milkiness appears which eventually merges into the yellow or purulent lesion. The size of the lesion has again increased slightly, but, except where confluence has altered the shape, the individual lesion preserves its circular base and rather full dome-shaped top. The red or pink areola so well marked during the earlier stage now gradually disappears. The change from vesicle to fully matured pustule may take from three to four days.

Desiccation.—In the most severe cases large areas of epidermis overlying the vesicles—more commonly on the back—almost slough off, as in an exfoliative dermatitis, leaving an exposed red raw surface. Such cases will often fail to reach a stage of desiccation. More favourably the pustules either rupture—when the skin is normally soft—or, particularly in the palms or soles, dry up without bursting. The exuded pus forms a hard brownish crust or scab which in confluent cases completely involves the face in a thick mask. Under the tougher skin of the hands or feet shrivelled brownish "seeds" are formed (Fig. 2) which can only be cleared by the slow process of opening up each lesion with a sharp needle or tenotomy knife.

Thus, in summary, the classical smallpox lesion may be described as uniform in size, regular in shape, and deep-set in the skin; progressing from stage to stage in a leisurely but inexorable fashion. In contrast, the lesion of chicken-pox shows much variation in size and shape, lies very superficially on top of the skin, progresses rapidly in 24 to 48 hours from papule to scab, and appears in a series of crops.

The Distribution

As has already been described, the earliest elements of the eruption appear on the forehead, face, and wrists. Thus at the outset the character of the distribution is announced by its predilection for the peripheral areas of the body (see Fig. 3). This is a diagnostic point of great importance and contrasts with chicken-pox, in which the lesions increase in number as the centre of the body is approached. But, although this general distribution will usually supply a valuable pointer to the diagnosis, just as much importance must be attached to the focal distribution: to the sites on which the rash is most concentrated as well as the areas which are avoided. Although the reason remains obscure, the smallpox virus shows a preference for skin cells overlying areas which are subject to trauma and minor irritation. The protection afforded by the clothing probably explains the

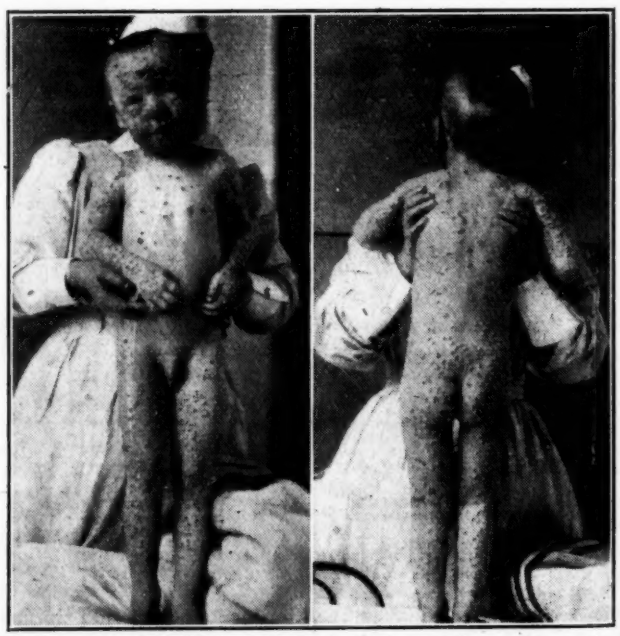

FIG. 3.—The distribution of the rash in smallpox. Note the heavy involvement of the face, the sparing of the abdomen, and the comparative freedom of the popliteal fossa compared with the front of the knee.

gross distribution. In examining the patient, especially when the rash is sparse, particular attention must be given to such sites as the malleoli, the mastoid process, the elbows, the line of well-marked tendons, and parts of the body abraded by tight- or ill-fitting clothing. Although the bony prominence itself is not infrequently devoid of rash, there is a tendency for the lesions to group themselves in profusion around it or to run alongside the line of trauma (see Fig. 4). In contrast, there may be a complete absence

FIG. 4.—The rash of smallpox. Note the grouping around the wrist and the lesions running along the line of a prominent vein.

of lesions from sheltered areas such as the flexures. The axilla, says Ricketts, is a mine of information. Whereas in smallpox it often entirely escapes, it is almost always affected in chicken-pox. In the latter infection the focal distribution is much more irregular and little preference is evident between the sheltered and the exposed areas.

It may be stated as a general rule that, on the body as a whole, the rash of smallpox prefers the upper to the lower—the forehead more than the face, the head more than the trunk, the arms more than the legs (Fig. 3). On the arms and legs the rash is more profuse on the extensor surfaces and on the lower parts—the hands and wrist more than the arm, the foot and ankle more than the leg. Sheltered areas tend to be spared. In chicken-pox many of these points are reversed, so that the arms and legs are spared rather than the trunk, flexor surfaces are involved as much as extensor, and hollows such as the axilla show no immunity. The whole picture is more erratic and variable.

[Part II will appear in our next issue.]

Refresher Course Book.—The first 55 articles of this series (fully revised) are available as a book, price 25s. including postage, from the Publishing Manager, B.M.A. House, Tavistock Square, London, W.C.1.

John Newport Langley, the centenary of whose birth falls on November 10, was a pupil of Michael Foster at Cambridge, and in 1903 succeeded him as professor of physiology there. His most important work was on the autonomic nervous system. He mapped out the sympathetic pathways to various organs and fixed the position of the relay cells upon their course. He also investigated the mechanism through which the nervous impulse starts the contraction of muscle fibre. With Gaskell he built up much of our knowledge of the sympathetic system. In 1878 Foster had founded the *Journal of Physiology*, but by 1894 it had become embarrassed by debt. Langley paid off the debt and became both owner and editor. This was an important event in British physiology, for Langley not only insisted that every paper published should be a contribution to knowledge, but he also set the high standard of form and style which has ever since been associated with that journal. He died on November 5, 1925.

DICKENS'S DOCTORS

A surprising number of doctors appear in the pages of Dickens, many of them anonymous, and a delightful dissertation on them was given by Mr. Bernard Darwin in the form of the David Lloyd Roberts memorial lecture to a distinguished audience at the Royal Society of Medicine on October 29. Dickens, he said, probably knew more about medicine than the ordinary layman of his time, and he evidently liked doctors. He had a great feeling for suffering, and in *Our Mutual Friend* gave a charming and not over-sentimentalized account of the Children's Hospital in Great Ormond Street. Later he gave a public reading of the *Christmas Carol* for that institution, and charmed about £3,000 out of the pockets of his audience. It was true that he laughed at doctors, but that was his way—perhaps his only way—of making his point. There were some ramshackle doctors among the doctors he depicted, but no sinister figures such as appeared among his lawyers, like Dodson and Fogg. Moreover, there were no murderers among his doctors, although at about the time he was writing *Little Dorrit* the exploits of Palmer of Rugeley were making an enormous impression on the public mind, including the mind of Dickens himself.

Bob Sawyer

In Mr. Darwin's opinion, far and away the most attractive of Dickens's medical creations was Bob Sawyer. There were two great moments in *Pickwick*, one in chapter 20 when the elder Weller made his first appearance, making Sam shrink into a little Cockney by comparison, and the other in chapter 30 at Manor Farm when Sam tells his master of the arrival of a couple of "Sawbones," one of whom was the redoubtable Bob. There were people who did not like Bob Sawyer, regarding him as a noisy and vulgar young man. But, after all, of what was he accused? Of smoking in the street, a practice which everybody followed to-day, and of calling waiters by their Christian names, a habit now not unknown in the highest circles. Too exacting a standard of manners was apt to be demanded. On the other hand, there were phases of his practice which might have been considered as "infamous in a professional respect." He sent his boy round leaving wrong bottles of medicine at houses in order to get himself known, and the same useful boy would call him out of church in the middle of the service on the presumption that a patient had been taken suddenly ill, making people exclaim what a practice this young man Sawyer (late Nockemorff) must have. But Bob Sawyer was a zealous doctor. When the Eatanswill editors had a fight, or when Mr. Winkle fell on the ice, Mr. Sawyer hovered round with his lancet, ready to bleed if necessary, and everyone would recall his wisdom when Mr. Pickwick fell into the pond and was taken home and put to bed and given unlimited quantities of hot punch. Bob Sawyer declared that there was nothing like hot punch in such cases, and that if hot punch did ever fail to act as a preventive it was because the patient had fallen into the vulgar error of not taking enough of it. In the end Bob Sawyer, with his inferior companion, Benjamin Allen, got surgical appointments with the East India Company, and, having each had yellow fever 14 times, resolved to try a little abstinence, after which they did well. Frankly, Mr. Darwin found it difficult to accept this termination, which was out of character. Dickens could not bear the unhappy ending. His characters must be cushioned and pensioned off. It was not altogether Dickens's fault. He did try in one of his books—*Great Expectations*—to have a different ending, but his publishers told him the public would not stand for it, and, of course, the customer was always right.

A Mort of Doctors

Dickens might have thought he had been rather hard on the medical profession in creating Bob Sawyer, and tried

to make up for it in *Bleak House* by creating Dr. Woodcourt—a thoroughly virtuous doctor, very considerate and kind, apparently attending all his patients for nothing, and showing great heroism in a shipwreck. But he was a character about whom nobody ever cared.

Almost every kind of doctor appeared at least briefly in the pages of Dickens. There was the fashionable physician, the respectable suburban practitioner, the country doctor. There were strange characters such as that medical scarecrow who brought little Dorrit into the world, and exclaimed, "I'm the boy," and took a comb from the chimney-piece and stuck his hair upright; and the doctor who had a peculiar way of smacking his lips and saying "Ah!" at intervals. There was the not very affluent doctor who suffered some little derogation of dignity by having himself to let down and put up the steps of his carriage. If Guy's could boast Bob Sawyer Bart's could boast Jack Hopkins, with his story of the child who swallowed the bead necklace, and in the hospital ward made such a devil of a noise with the beads rattling inside him that they were obliged to muffle him in a watchman's coat. One notable "doctor," who had no qualifications at all, was Alfred Jingle, Esquire, who carried a stomach pump in his portmanteau. Then, still in *Pickwick*, there were Dr. Slammer of the 97th and Dr. Payne of the 43rd. The original of the former was a real doctor, who married Miss Barrow, Dickens's aunt. Of the many anonymous doctors one should not forget those who figured in *Nicholas Nickleby* and who doubted, according to Fanny Squeers, whether her father "would ever recuvver the use of his legs, which prevents his holding a pen." There was also the doctor who awaited the appearance into the world of David Copperfield and had a notable encounter with Miss Betsy Trotwood.

The pages of Dickens, said Mr. Darwin, contained a large number of feeble-minded people, not always attractive, though here he made a great exception of Mr. Dick; and he shared the general feeling with regard to some of Dickens's death-bed scenes, though there was one which he thought full of real dignity and pathos—namely, the elder Weller's account to his son of the death of Mrs. Weller.

The David Lloyd Roberts lecturer is appointed in turn by the Royal Society of Medicine, the Royal College of Physicians, and the Medical Society of London, and this year it was the turn of the first-named, whose President, Dr. F. M. R. Walshe, was in the chair. Lord Webb-Johnson moved a vote of thanks.

Nova et Vetera

LEECHDOM

Anglo-Saxon Magic and Medicine. By J. H. G. Grattan and Charles Singer. Illustrated specially from the Semi-pagan text "Lacnunga." (Pp. 234; illustrated. £1 8s.) Published for the Wellcome Historical Medical Museum by Geoffrey Cumberlege (Oxford University Press). 1952.

The literature of Anglo-Saxon medicine is relatively sparse. Little, indeed, has been added to our knowledge of this subject since the appearance, in 1864–6, of the three noteworthy volumes by the Rev. T. O. Cockayne, entitled *Leechdoms, Wortcunning, and Starcraft of Early England.* The present work, produced by the collaboration of the leading Anglo-Saxon scholar of his time, the late Professor Grattan, and the eminent historian of medicine, Professor Charles Singer, is all the more welcome. The first half of the book is a general survey of magico-medical practice in Anglo-Saxon England, while the second half consists of a translation, with notes and glossary, of the "Lacnunga," a collection of medico-magical recipes, charms, and invocations, written about the year A.D. 1000 and surviving in a single manuscript—namely, British Museum Harley 585. The translation will probably prove more interesting to the philologist than to the medical man, but the survey contained in the first 94 pages is of supreme value to the medical historian, and throws a flood of light upon what has hitherto been a dark corner of medical history.

Anglo-Saxon medicine cannot be said to have any rational basis. The Lacnunga hardly emerges from the barbarian world of magic, and it can in no sense rank alongside the works of Bede (d. 735) and Byrhtferth (d. *c.* 1020), who stand the one at the beginning, the other at the end, of the Anglo-Saxon literary period. On the contrary, it represents the last degenerating remnant of the great system of Greek medical thought. The wisdom of one generation may become the folly of the next. Prayers, liturgies, and sacred works are often misunderstood, and then, becoming corrupt, are put to magical uses. Of all cultural expressions, magic passes most rapidly from people to people. The "leech" who wrote the Lacnunga was not of the priestly class, and is never shown as "tonsured" in the illustrations. His collection of remedies is arranged in the age-long plan of beginning with the head and working downwards. More than 100 plants are mentioned, and many can be identified, but greater stress is laid upon the charm or incantation which is to accompany the remedy than upon the remedy itself. To the philologist, the medical historian, and all in search of new knowledge this worthy successor to Cockayne will be found indispensable.

DOUGLAS GUTHRIE.

Preparations and Appliances

FLOSS NYLON—PRELIMINARY REPORT

Mr. A. K. MONRO, lecturer in surgery, Postgraduate Medical School of London, writes: Nylon was first used in surgery six years ago. Fear was then entertained that, like so many of its non-absorbable predecessors, it might perpetuate infection occurring in the wound—in fact that such wounds would not heal until the nylon had been extruded. In the intervening years nylon has been used in a considerable number of cases, with promising results. Evidence has accumulated to show that such wounds may in fact heal without extrusion of the nylon. The theory was advanced that this was owing to its monofilamentous form.

Monofilament nylon, however, has the disadvantage of slight rigidity and of not being entirely pliable. Knots do not tie down tightly and are apt to slip. To prevent this, three or four knots are tied, leaving an undesirable mass of suture material which can sometimes be palpated after the wound has healed. Braided nylon is more pleasant to work with, but again it has slight rigidity and single knots are unreliable.

Floss nylon, composed of fibrils of approximately the same size and in the same number as the silk fibrils in floss silk, overcomes these disadvantages. It is entirely pliable, soft, smooth, easy to work with, and it can, of course, be boiled repeatedly; a knot tied down as a reef does not slip. It was first used in 1948, when a small quantity of it was obtained, as a lattice repair in seven cases of inguinal hernia. These all healed cleanly and have remained sound. More recently the supply has been increased, and it has been used both in the repair of herniae of all kinds and for the closure of abdominal incisions. Here, in infected wounds, it has been seen to allow healing without subsequent extrusion of the nylon.

Floss nylon combines the advantages of floss silk with the inertness of nylon, and may well prove to be a valuable material in the repair of hernia. I am most grateful to Mr. Proudfoot, of Messrs. John Bell and Croyden Ltd., for his courtesy and care in the production of it.

Correspondence

Because of the present high cost of producing the Journal, and the great pressure on our space, correspondents are asked to keep their letters short.

Kwashiorkor

SIR,—The patient and persistent efforts of Drs. H. C. Trowell, R. F. A. Dean, and J. N. P. Davies (October 11, p. 791) in Uganda to locate the exact nutritional origin of kwashiorkor deserve our respect and admiration. The value of milk in the treatment of the acute disease had already been recognized, but Dr. Dean's results appear to show that it is the protein which is the effective curative agent. These findings, coupled with our knowledge of the social and dietary habits of native populations, appear at first sight to incriminate protein deficiency as the cause of kwashiorkor.

Having left this field of work some time ago, I feel diffident about commenting on the observations of those whose minds are refreshed by constant bedside contact with the disease. At the same time they have, with your editorial support, committed themselves deeply to a point of view which, if correct, will make the eradication of this disease a wellnigh hopeless problem in this generation. If, as they contend, kwashiorkor has its origin in protein deficiency, what chance is there of supplying this deficiency in our time? With the prevalence of animal trypanosomiasis in West Africa there is no possibility of establishing herds to provide sufficient meat or milk there for many years. Even if Dr. Dean's hopes are justified and vegetable protein solved the problem, it would take years of effort to switch the population on to the cultivation of soya beans for their dietary staple. May I therefore put forward a few points to show that the vitamin-deficiency theory of the origin of kwashiorkor should not be discarded for the moment?

Would not a clinician who examined a case of rickets find plenty of evidence of "malignant malnutrition" and protein deficiency at the florid stage? And yet rickets has been abolished in this country at very little cost by vitamin supplements. The fact is that any form of disease which leads to inanition is likely to end in a syndrome of protein deficiency. It may be argued that in kwashiorkor we know the diet is defective in protein. But are our standards valid? Do not some of the finest physical specimens of the human race come from the same region where kwashiorkor flourishes?

It is possible that the kwashiorkor seen in Uganda differs from that seen elsewhere, although it is equally possible that each of us, blinded by his own prejudice, sees in kwashiorkor that which he sets out to observe. I am intrigued, for example, by an important omission in the description of the hair in kwashiorkor in Uganda. In West Africa the most startling feature—to me—was the fact that the hair was falling out and could be pulled out painlessly in bunches. This gave a moth-eaten appearance to the scalp. This symptom, which impressed me as characteristic of severe kwashiorkor, is either of no significance to the Uganda observers or else does not occur in the local disease.

The authors do not mention the resemblance between the patterns of the kwashiorkor dermatosis and that of gaol "pellagroid." Here again I was interested—possibly to the point of prejudice—in the similarity of the two dermatoses. The pellagroid which occurs in gaols and asylums can be prevented, as Landor and Pallister[1] showed, by the addition of minute amounts of yeast to the diet. This has been amply confirmed. In one gaol in West Africa I found that the bitter local spinach was first boiled and then squeezed to get out a bitter principle. The water in which it was boiled was thrown away and the spinach was then added to the rest of the boiling stew. By merely stopping this practice the incidence of the orogenital pellagroid fell to vanishing point. Now the pattern of the adult pellagroid is complete in the rash of kwashiorkor. The Uganda observers ignore the significance of this and describe the evolution of the rash as if it could be accounted for by chance traumata. Here again it may be a question of prejudice or—to put it more mildly—point of view. I saw in this pattern of the kwashiorkor rash the imprint of ariboflavinosis. Possibly I was prejudiced by the fact that 12% of the poorer classes in Lagos from whom we got our kwashiorkor cases showed this evidence of riboflavin deficiency. Once more, does the kwashiorkor of Uganda differ from that of West Africa in its background of ariboflavinosis?

Dr. Trowell mentions the sudden death which is such a tragic and mysterious feature of kwashiorkor. Williams[2] has already described this in association with fatty liver in West African cases. I[3] described it in my own cases and pointed out that Sebrell[4] had also noted the association of yellow liver and sudden unexpected death in his experimental dogs—which brings us back again to ariboflavinosis.

Finally, in spite of his belief in protein deficiency, Dr. Dean records that a diet of low protein content cleared up the symptoms in one of his cases even though the blood protein was not raised.

In 1946 I saw a good deal of malnutrition in post-war Germany. I saw many cases of nutritional oedema, some of whom were children. But I saw no skin lesions remotely resembling pellagra or pellagroid in adults and no case of kwashiorkor in children. It will be readily admitted that the whole population was suffering from inadequate protein and calories. Why were there no cases of kwashiorkor?

I have not found that riboflavin cures kwashiorkor. It would be as unreasonable to expect a cure from riboflavin or the B_2 complex as it would be to expect a cure of rickets by vitamin D. The protein diets used so successfully by Dr. Dean also contained adequate amounts of the vitamin-B_2 complex. While the authors have put forward strong arguments in favour of a primary deficiency of protein in the diet, I feel the question is not yet finally settled. It is still possible that a daily vitamin supplement supplied by food yeast would prevent kwashiorkor. Because the cost of such a supplement is negligible, and the technique of production and distribution not very difficult, it deserves further consideration.—I am, etc.,

Bristol. WILLIAM HUGHES.

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First-aid Treatment for Nerve Gas Poisoning

SIR,—It has been brought to my attention that anti-gas ointment will not be issued to Civil Defence sevices, and hence the advice given about decontamination in the penultimate paragraphs of the article entitled "Chief Characteristics of Nerve Gas with Notes on First Aid Treatment" (August 9, p. 334) may not always be apposite.

In circumstances—for example, in civil life—where adequate supplies of water are available and the contaminated skin can be speedily and thoroughly cleansed, washing is an effective means of decontamination for both nerve and mustard gases. If speedily applied there is, in fact, no better method for nerve gas. In Civil Defence practice any liquid contamination on the skin is speedily removed by wet swabs and treatment is continued by thorough washing with plenty of water and soap.

Anti-gas ointment is, however, provided for Service personnel, since under active field service conditions adequate water supplies for washing may not always be immediately available.—I am, etc.,

Ministry of Supply. H. M. GARNER, Chief Scientist.

Acute Radiation Syndrome

SIR,—Your leading article on the acute radiation syndrome (October 25, p. 925) is of great importance in the assessment of radiation injury. Misunderstanding may arise as regards the dosage received by the victims of the accident at Los Alamos from the fact that you omit to mention the greater biological effectiveness of neutrons compared with *x* rays, which has been accounted for by the authors in some of the figures you quote, but not in others. The authors of the original article assumed neutrons to be five times as effective biologically as an equal physical dose of *x* rays, so that, although the actual energy absorption in the fatal cases is about 9 megagramme-roentgens, it might be expected to be as effective biologically as a dose of 16.5 megagramme-roentgens of *x* rays.

During work which has been carried out by the Medical Research Council on the effects of a single dose of *x* rays on the symptom pattern of radiation sickness and its physiological disturbances, it has been found that in many instances doses of up to 5 megagramme-roentgens of *x* rays can be given to the whole trunk with only transient symptoms of sickness and certainly no evidence of the more serious accompaniments of the acute general radiation syndrome.—We are, etc.,

W. M. COURT BROWN.
L. H. GRAY.
R. F. MAHLER.

London, W.12.

Rotten Teeth

SIR,—In the annotation on "Rotten Teeth" (October 25, p. 928) it is stated: "The two common dental diseases, caries and pyorrhoea, are diseases of civilization." There is ample evidence that this is true of caries, but I would be glad to know on what grounds civilization can be blamed for so-called pyorrhoea. A high incidence of the latter disease, using the term pyorrhoea in its wider sense, can be found alike among ancient skulls and existing primitive races. One of its prominent causative factors is salivary calculus, which in turn is generally believed to be common to both primitive and modern dentitions. I am particularly interested in the incidence of calculus and would be most grateful for references to any reputable investigations which have clearly associated primitive conditions, environmental or dietetic, with relative freedom from calculus.—I am, etc.,

J. D. KING.

Dental Research Unit, Medical Research Council, King's College Hospital Medical School, Denmark Hill, S.E.5.

Banti's Disease

SIR,—It is a pity that Sir Henry Tidy (July 5, p. 1) is so emphatic in proclaiming Rh incompatibility as the cause of Banti's disease. One wonders if he is not too dogmatic in stating that all cases are due to erythroblastosis. I have seen one case in which the patient and the mother were Rh-positive. Three years ago, I believe, it was reported that two Australians had investigated the Rh factor in some cases of Banti's disease and several showed Rh incompatibility. They suggested it might be a contributory factor.

It would be interesting to know the family history of jaundice, hydrops, stillbirth, etc., and the actual Rh of Sir Henry's patients with Banti's disease, as these findings might add substantially to his claim. I myself have seen one child with Banti's disease who was Rh-positive and the mother Rh-negative, and one other child with aplastic anaemia in a family with a strong history of jaundice and stillbirth who was Rh-positive and had an Rh-negative mother.

However, to say that all Banti's disease is due to erythroblastosis without complete laboratory evidence of incompatibility is rather like describing cases of syphilitic osteitis without including a positive blood serology.—I am, etc.,

DEREK B. WILLIAMS.

Rochester, N.Y.

Infected Anaesthetic Apparatus

SIR,—I have long felt that the danger of tuberculosis transmission from anaesthetic machines is a real one. It is easy for an unrecognized case of pulmonary tuberculosis to find its way into a routine surgical list. How can we be certain that the rebreathing tube of the anaesthetic machine will not be infected, and, in the case of "circle" absorbers, the whole apparatus, with consequent risk to succeeding patients? Your annotation of October 18 (p. 873) dismisses such suspicions as unreasonable, while conceding that "it would seem worth while to sterilize the inside of the closed-circuit apparatus when practicable." The literature on the subject of infected anaesthetic apparatus is confusing. Some hold that tubercle bacilli are filtered out by the soda-lime of carbon-dioxide absorber units,[1] while in the work cited by your annotator[2] pathogenic organisms passed freely through soda-lime. In the latter study tubercle bacilli were not introduced, but the fruitful harvest of other organisms suggests that tubercle bacilli would have been recovered if they had been introduced.

It is high time that a carefully planned investigation was made by a competent team well qualified to give an authoritative answer to the question of tuberculosis transmission by anaesthetic apparatus. In my opinion current sanitary practice with anaesthetic machines is slovenly and dirty up and down the country, and I believe that in some places rebreathing tubes and reservoir bags are not even washed from one week's end to the next. I think it is a pity that this ostrich attitude to a potential hazard should be encouraged through the medium of your official columns.—I am, etc.,

P. R. BROMAGE.

Emsworth, Hants.

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Pulmonary Tuberculosis in the Rhondda Fach

SIR,—Drs. A. L. Cochrane, J. Glyn Cox, and T. Francis Jarman (October 18, p. 843) have presented a very good account of an excellent piece of investigation, and there are many lessons that we can learn from it. I would like to comment on a few of these. There has been considerable complacency since the pulmonary tuberculosis death rate began to fall steeply. This article should do much to get rid of such an attitude. The prevalence of the disease in young women is almost startling when we realize there are 35 active cases per thousand at the age of 25. As you state in your leading article, this probably applies to many urban areas within the British Isles. Surely we cannot delay any longer instituting real preventive measures and insisting that B.C.G. vaccine is both used for this very susceptible group and also manufactured in this country. We have spent the last 30 years discussing whether any action should be taken—surely these figures are sufficient justification for passing on to the next stage.

When we look at the provision for treatment it is pathetic to realize that over 60% of both males and females, already known to have tuberculosis, had never been in hospital. We must presume that this same state exists throughout the whole of South Wales. If so, it is a serious reflection on those responsible for hospital facilities. In 1948 the medical profession gained the dominant position it had been demanding on regional hospital boards and management committees. Consequently it must bear a considerable responsibility for this state of affairs, and I think it is true to say that very few general surgeons or physicians, with such positions, have pressed the claims of the tuberculous patient.

It is stated in the article that at Tyntyla Hospital "facilities for thoracic surgery were not available, but the few cases which required it were transferred to Sully Hospital or elsewhere for this purpose." When I was in Cardiff, four months ago, the senior thoracic surgeon for South Wales told me that patients were waiting for two years for thoracic surgery, and this included some of the cases discovered in the investigation. The main reason for this

delay was the great shortage of nurses, and I understood that the general hospitals, including the teaching hospitals, were not seconding any nurses for the treatment of tuberculosis. The resistance of matrons and other nursing administrators to the suggestions made by the Minister of Health have been such that we must think very seriously of diminishing their power to prevent reasonable use of our nursing personnel.

Turning to the problem of pneumoconiosis, we find a very disturbing picture revealed. The peak of 56% of all miners showing evidence of dust disease at the age of 40–44 does not suggest this is mainly a disabling disease. Miners themselves do not believe this to be true. We could know the truth of the suggestion if the age at death of men in South Wales suffering from pneumoconiosis had been published with other data given. It is essential that the truth be known so that full preventive measures can be taken. This cannot happen until the whole unhappy picture has been painted. Miners will not encourage their sons or relatives to enter an industry in which so many of their friends have become disabled and subsequently died before the age of 50.—I am, etc.,

London, N.W.10. HORACE JOULES.

Harrow and Wealdstone Train Disaster

SIR,—As I have been unable to obtain a complete list of all the doctors who rendered aid to those injured in the unfortunate train accident at Harrow and Wealdstone on October 8, I should be grateful for the opportunity to send my sincere thanks to all of them through the medium of your *Journal*.

I know the names of some of them, of course, whilst others preferred to remain anonymous, but in keeping with the highest traditions of the medical profession all of them rendered such invaluable aid that it is impossible to estimate how many more lives would have been so tragically lost had it not been for the medical attention given to them either before or immediately after they were brought from the wreckage.

I should like each and every doctor concerned to accept my very sincere and grateful thanks.—I am, etc.,

J. W. WATKINS,
Chief Regional Officer,
Railway Executive, London Midland Region

Rheumatic Fever

SIR,—We are entirely in agreement with Mr. M. J. H. Smith's letter (October 4, p. 776) that the available experimental evidence by no means proves that salicylates engender adrenocortical excess, and we stated nothing to the contrary in our paper. The hypothesis that salicylates have this action need not be discarded because of the results of the important experiments quoted by Smith. These experiments were carried out in rats and were concerned with only one aspect of salicylate action—namely, carbohydrate metabolism. On the other hand, there are many points of similarity in the action of salicylates and A.C.T.H.

We believe that the theory is very useful to the clinician in the management of rheumatic fever, particularly in the dosage and duration of treatment. Perhaps most important of all is our suggestion, derived from this theory, that a low sodium diet be given with salicylate treatment, and that the sodium salt be avoided.—We are, etc.,

F. BACH.
A. FREEDMAN.
L. BERNSTOCK.

London, E.9.

Vertigo

SIR,—Twenty years ago in a country practice an elderly male patient, panting because of early heart failure, presented himself at the surgery complaining of giddiness. His doctor was ill, and the young locum noticed shortness of breath and the swollen legs, and found the blood pressure to be elevated, and treated him for his cardiovascular troubles. Although the breathing improved and the swelling of the legs became less, the patient seemed dissatisfied when, after several weeks of treatment, he was still having severe attacks of giddiness.

On one occasion the patient called when the locum was at a confinement and the old doctor had left his bed to take the surgery. The young doctor returned to find his elderly colleague syringing the ears of his patient. "Remember, my boy," he said, "that the commonest cause of vertigo is wax in the ear."

The intervening 20 years have abundantly justified the truth of that aphorism, and it is surprising to find no mention of wax as a cause of vertigo in the otherwise excellent Refresher Course article by Mr. Terence Cawthorne (October 25, p. 931).

Another fairly common cause which seems to have been overlooked is foreign body in the meatus—the forgotten pledget of cotton-wool, the bead, the moth or other insect.—I am, etc.,

Cirencester R. E. HOPE SIMPSON.

SIR,—In Mr. Terence Cawthorne's excellent article on "Vertigo" (October 25, p. 931) there was no mention of neck injuries as a cause of vertigo. In nearly 10% of his cases there was a history of injury, particularly head injury, and the explanation offered was that the labyrinth was damaged by the shake-up. This may well be so, but I would offer another explanation. When a person receives a blow on the head there must be a transmitted jar to the neck. This is especially so when the blow is anticipated. The person makes an attempt to avoid the blow or braces against it, and in either case the cervical joints are jerked.

In most of the cases of vertigo which I have seen there is evidence of joint fixation or subluxation, and, when the injury was sustained years before, osteoarthritic changes have supervened. The type of person whom I see is the individual who has failed to recover with ordinary methods of treatment, and they wonder if manipulative measures will help. Therefore I tend to see mainly those with a history of trauma.

There is not the slightest doubt that manipulation of the cervical joints can relieve vertigo in suitable cases. How cervical joint strain causes vertigo I do not know, but it is a fact, and it should be added to the list of aetiological factors in vertigo.—I am, etc.,

London, W.1. ALAN STODDARD.

Ichthyosis and Hypnosis

SIR,—Dr. John Freeman and I seem to have been at cross purposes in our last letters (October 11, p. 832). I would not hesitate to agree with him about the influence of the emotions on "hay fever, asthma . . . and all that lot." However, at the risk of tiresome repetition I must again say that we are discussing congenital ichthyosiform erythrodermia of Brocq and not "all that lot."

I have diligently read all the references Dr. Freeman suggests as well as other textbooks, both on allergy and dermatology.[1–6] I have also conducted quite an exhaustive search on the special literature relating to this condition, and as yet have found no suggestion whatsoever that this condition is ever allergic or has ever been described as being affected by the emotions.—I am, etc.,

East Grinstead, Sussex. A. A. MASON.

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SIR,—I wish to apologize to Dr. John Freeman (October 11, p. 832) for my ignorance of the very considerable thought he has given to the ambiguity of the word allergy, and to have quoted (September 27, p. 725) a passage he knows so well. However, after reading his four references I am still not convinced that congenital ichthyosis can use-

fully be included in the group "toxic idiopathies." Existing alone, without any other concomitant allergic disorder, congenital ichthyosis does not fulfil Dr. Freeman's own postulates for inclusion in this group.

He gives "seven manipulable causes: heredity, idiotoxin (the specific poison), idioceptor (the patient's sensitivity), trauma, bacteria, and the emotions." He concludes that "none of these seven causes can ever operate alone, and all seven of them are necessarily involved in every case to a greater or lesser extent." He further states that characteristically the idiopathies "wax and wane," a "serious leak" always occurs, and that one disorder may be supplanted by, or converted into another—for example, eczema followed by asthma, "epilepsy turned into asthma by the intervention of whooping-cough," etc.

It would appear from the foregoing that the cases of ichthyosis seen in Dr. Freeman's allergy clinic constitute a different entity from those met in a dermatological department. Ichthyosis by definition is a congenital, cutaneous disease characterized by a dry, harsh, scaling condition of the skin associated with abnormal cornification. It commonly develops shortly after birth, progresses steadily, becomes stationary after a passage of time, and is resistant to all forms of treatment. It does not wax and wane (although exacerbated by cold), nor when found alone (as in Dr. A. A. Mason's case) ever alternate with any other allergic disorder. A "serous leak" cannot be demonstrated, nor has an idiotoxin, idioceptor, or bacterial factor ever been found. The role of emotions is obscure, the causal shock to be sought in genetic or intrauterine transference from parent to foetus. This is a possibility, but rather beyond the "emotional starters" described in Dr. Freeman's book, *Hay Fever*.

I fully endorse all Dr. Freeman says about the effect of the emotions on "toxic idiopathies"; this is not in dispute. Indeed I should go further and include the influence of the psyche in all illness. However, I have failed to discover any reference to purely emotional factors having either aetiological or phasic influence on ichthyosis congenita. Dr. Mason's patient has lived full 16 years, and presumably has felt many emotions, none of which has had the smallest effect on the condition of his skin.

We are considering a most severe and static case of congenital ichthyosis which has been markedly improved by hypnotic suggestion acting through the psyche along pathways unknown. This remains an unprecedented and inexplicable fact.—I am, etc.,

London, S.W.1. KATHRYN COHEN.

Method of Estimating Cerebrospinal Fluid Glucose

SIR,—We were interested to note the method of glucose estimation in the cerebrospinal fluid used by Dr. R. W. S. Harvey (August 16, p. 360). Such a test may be used for screening, and in our experience only differentiates a low from a normal glucose, whatever the underlying pathology. We do not agree that the test can be regarded as being in any way specific in the diagnosis of tuberculous meningitis, as might be inferred from his article.

We would suggest further that a precise estimate of the glucose level in the cerebrospinal fluid is essential on the following grounds. First, it assists in the diagnosis of an early case, where the level may be so near normal as to reduce Benedict's solution, in that it allows correlation with the blood glucose level and permits observation of a falling C.S.F. glucose on serial lumbar punctures. These two factors were of material assistance in a recent case of ours in which the diagnosis was subsequently confirmed at necropsy. Secondly, it may be of value in assessing the progress of a case under treatment and determining the value of the therapeutic regime employed.—We are, etc.,

J. F. WEBB.
G. H. ISAAC.

British Military Hospital, Hong Kong.

Complete Rupture of Duodenum

SIR,—Having seen in recent months two reports of cases of partial rupture of the duodenum due to direct violence, I am sending you particulars of a case of complete rupture of the third part of the duodenum which came under my care in 1951. The following is a brief history of the case.

The patient, aged 21, a member of the R.A.F. Regiment, was out on patrol in a scout armoured car. At the time he was acting as wireless liaison man and was standing in the turret of the car, his body and head above the turret rim. A collision occurred and he was thrown violently against the turret rim. He was at once seized with a very violent abdominal pain, and on being removed from the car he fainted. He was then brought to hospital, which he reached about 1½ hours after the accident had occurred.

On admission it was quite obvious from his condition that a gross intra-abdominal injury had occurred. His abdominal wall was rigid, his pulse was 120, and he was sweating profusely. A blood transfusion was at once given and very shortly afterwards he was put on the table.

On opening the abdomen the first thing noticed was a very large extravasation of blood; this was rapidly cleared by mops and suction. The liver and spleen were at once palpated and found to be undamaged, but a large tear in the gastro-colic omentum was seen. All bleeding points in this were picked up and tied. The stomach, pylorus, and first and second parts of the duodenum were found to be intact. On lifting up the transverse colon a considerable amount of undigested food, composed chiefly of raisins, was seen. On further mopping up, this food was seen to be issuing from a recessed aperture from which a small portion of bowel mucous membrane was protruding. Traction on this at once revealed what was the proximal end of a complete duodenal tear just short of the duodeno-jejunum junction. Approximation of the two ends and end-to-end anastomosis were carried out. A jejunostomy was then done and two abdominal drains were put in, one to the actual sewn suture line and one to the pelvis.

He had a very stormy convalescence for the first five days, but ultimately settled down, with the exception of some griping pains. He improved sufficiently to be sent to a convalescent home four weeks after the day of operation. He was fed by jejunostomy for ten days.

While at the convalescent home he had a further attack of severe abdominal pain, but this settled down after a few days of very careful dieting. A bismuth meal showed no obstruction whatsoever at the line of junction.

The latest report on him is that he is quite fit and can eat anything without any adverse after-effects, and he is doing normal duty.

During a period of 27 years' surgical practice this is the first occasion on which I have seen an injury of this type, and I have been unable to trace any other case of similar nature in the literature.—I am, etc.,

Bishop Auckland, Co. Durham. D. R. E. ROBERTS.

Morbidity Statistics in General Practice

SIR,—I have been studying Dr. John Fry's excellent article on morbidity in his practice on the south-east outskirts of London (August 2, p. 249). I was particularly interested in his Table VII of morbidity statistics per thousand population, since I prepared similar statistics of illnesses treated in a practice of 2,864 patients in Nakuru, Kenya, over a period of nine and a half years.[1] Like Dr. Fry, I also compared my figures with those of the Social Survey of Sickness.[2] The statistics of Dr. Fry are, however, not all strictly comparable with those of the Social Survey, since the latter were mainly drawn from individuals over the age of 16 years, whereas the former were presumably taken from persons of all ages.

Comparative statistics of long-duration illnesses per thousand population over the age of 16 from the Nakuru district of Kenya over a period of nine and a half years and for England and Wales (monthly prevalence rates supplied by the Social Survey of Sickness) were published in a table. There was a close similarity of the figures in the case of cerebral vascular lesions, diabetes, peptic ulcer, and cataract. The table suggested that hypertension was more common in Nakuru and that disseminated sclerosis, rheumatic heart disease, pernicious anaemia, rheumatoid arthritis, and tuberculosis had a higher incidence in England and Wales.

Comparative statistics per thousand population for Nakuru district and for Stirlingshire Hospital admissions[3] were also tabulated and revealed a greater prevalence of gall-bladder disease, nasal sinusitis, and typhoid fever in Kenya, but a lower incidence of rheumatic fever and diphtheria.

It would be of value to compare the morbidity statistics in Kenya with those of Dr. Fry in England and of Dr. McGregor[4] on the Scottish border, and I hope to publish tables of comparison at a future date.—I am, etc.,

Nakuru, Kenya. A. D. CHARTERS.

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Faith and Functional Illness

SIR,—In every doctor's surgery these days there are a large number of patients whose complaints arise from deranged function rather than from true structural disease. The normal physiological function is deranged as the result of the nervous system being called upon constantly to work at full pressure and without respite, and the patient lives in a state of constant inward tension. To arrive at the diagnosis "functional" without making occasional serious mistakes necessitates extensive and expensive investigation if organic disease is to be excluded. Where true disease is excluded, selected functional cases are often referred for psychiatric treatment, which may help but does not always cure. It seems, then, that in these cases the doctor can only offer sympathy and reassurance and resort to the inevitable bromide or phenobarbitone.

The question arises—Is there any other way a tension state may be relieved? We think there is. To-day, far too many ignore the Christian faith and the existence of God. If only this faith could be resurrected in their daily lives it would reveal to them, *if they are willing*, the true meaning and purpose of life, and give them the strength and determination to meet and overcome the difficulties and frustrations of each day. Faith in oneself can come only through constant contact with one's own Church, where inward calm is born in the quietness of worship—not from drugs.

When true disease can confidently be excluded, a doctor's duty must end only after he has explained that the complaint is not of medical or surgical origin, and that the cure is more likely to be found in the patient's church than in the consulting-room. "Study to be quiet," said Izaak Walton. How right he was. God can heal so often where a doctor fails.—We are, etc.,

G. A. POWELL-TUCK.
Knowle, Warwickshire. N. J. RENSHAW.

Atmospheric Pollution

SIR,—Strong evidence has been presented supporting the contention that the inhalation of air polluted with coal smoke increases the incidence of respiratory disease,[1] particularly bronchial carcinoma. During the past three years I have been investigating the effects of coal smoke pollution gases on plant growth. As a botanist it is with some trepidation that I write to suggest some medical implications of my findings.

Sulphydryl compounds stimulate growth by increase in cell number.[2] Partially oxidized sulphur radicles inhibit cell division, the actual rate of cell division being to some extent controlled by the relative concentrations of these radicles and sulphydryl compounds.[3] This system is common to both plants and animals. The commonest and most abundant gaseous constituent of coal smoke pollution is sulphur dioxide. If plants are grown in polluted air containing this gas, their growth rate is less than that of plants grown in pure air.[4] If plants are subjected to pollution for only part of each 24-hour period their growth rate is higher than that of plants treated with pure air. It is thought that the sulphur dioxide contained in the polluted air becomes dissolved inside the plant and increases the concentration of partially oxidized sulphur radicles. If this situation persists growth is inhibited, but if the plant is moved from polluted to pure air the concentration of partially oxidized sulphur radicles is reduced by oxidation and reduction, and the sulphydryl compounds that accumulated in polluted air as a result of the blocking action of the partially oxidized sulphur radicles are freed to stimulate growth.

It may be that sulphur dioxide affects humans in a similar manner to that in which it affects plants. Continuous breathing of polluted air would adversely affect the replacement of lung epithelium and possibly lead to a greater susceptibility to respiratory disease. Lung cancer is abnormal growth of the bronchial epithelium. If air pollution does act in the manner suggested it is easy to see how it may lead to this form of cancer.

I trust that the above suggestions may prove helpful to those engaged on relevant research and be of interest to those concerned with public health.—I am, etc.,

Manchester. J. K. A. BLEASDALE.

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Block for Bisecting Kidneys

SIR,—This block has been designed for bisecting kidneys in the post-mortem room. It is made from hard, well-seasoned wood, and consists of two vertical pieces firmly fixed to a horizontal base and shaped at their upper ends to form a concavity in which the kidney rests (see Figure). The concavity measures approximately 4 in. (10 cm.) long, 1 3/5 in. (4 cm.) across its widest part, and 9/10 in. (2.3 cm.) down its deepest; the cleft dividing the two halves is 2/5 in. (10 mm.) wide.

The kidney is placed in the concavity, with the pelvis down and the ureter hanging freely between the vertical arms. A preliminary cut, about ½ in. (13 mm.) deep, is made in the presenting convex border, and the kidney, firmly held into the concavity by the thumb and fingers of the left hand, is then bisected by cutting downwards towards the hilum with a brain knife, preferably in one sweep from heel to point.

The use of the block not only allows a clean-cut section through the median line with a flat face free of wave marks, but also avoids the risk entailed to the palm of the left hand in the usual method of cutting a kidney. The flat face is desirable if a museum specimen is to be made, and, since it is probable that twisting of the kidney during cutting loosens the tubular epithelium, the use of this block should also improve the histological results. It has proved a useful aid in the post-mortem room.

I would like to thank Professor A. C. Lendrum for his helpful advice, and Mr. P. Harrison for photographing the block.

—I am, etc.,

Bradford, Yorks. R. A. MCINROY.

Appendicitis in the Non-European

SIR,—Mr. H. M. Karn's interesting comments (September 6, p. 566) upon Mr. Aubrey Leacock's article on appendicitis in the West Indies have prompted me to examine my own figures for this area of Zululand. This country hospital serves a population of some 40,000 Zulus and Basuto. The occupation is mainly pastoral, with 70% of the young men making periodic migrations to the cities for mining and industrial work.

Incidence of appendicitis is low, although actual figures are for obvious reasons difficult to come by. I have been responsible for eight cases which have come for operation in the period October, 1949, until the present, out of a total admission (medical, surgical, and obstetrical) of 5,162 persons. It is emphasized that this figure does not represent the incidence in the whole population, but the proportion of cases of appendicitis among those who would use the hospital in an emergency. In addition there are from time to time mild cases which remain unconfirmed owing to my own and the Zulu's unwillingness to indulge in promiscuous surgery. It appears quite justifiable to treat these cases conservatively among the Bantu, although chronic cases coming ultimately to surgery occur here as elsewhere.

Age incidence does not differ from that among Europeans, but there is a bias in favour of the educated. Nevertheless, the most severe case I have operated upon here was in a tribal youth.

I do not know why the incidence is low among Africans in this part of the world. Diet would appear to be the easiest explanation of the great difference in incidence here from that seen in the West, but one remains sceptical until further evidence is put forward. A bulky maize diet is the lot of our Zulus, whether rich or poor, educated or uneducated. There is a slight increase in the amount of meat consumed by the better educated, which may perhaps be of importance.—I am, etc.,

Nqutu, Zululand. E. A. BARKER.

Smokers' Cough

SIR,—Dr. R. D. Summers and Mr. J. C. Gilmour, of Messrs. Godfrey Phillips Ltd. (October 18, p. 881) accuse me of having made "misleading statements" in my letter (September 20, p. 670) on this subject. The only statement I made was that self-made cigarettes do not make me cough. My inference therefrom that suspicion fell upon the paper was not made without considerable experimental grounds. These, briefly, are: (1) Machine-made cigarettes broken down and re-rolled in thin paper appear to be far less cough-making than in their original state. Many correspondents have confirmed my own opinion on this. The objection may be raised that it is necessary slightly to dampen the tobacco before re-rolling, by enclosing it with a piece of cut potato, or some similar means, thereby diminishing the dust factor; but (2) machine-made cigarettes provided with a dust-removing filter still appear to be more irritating than the home-rolled kind. (3) At least one brand of manufactured cigarette made with thin paper appears to have much the same characteristics as the self-made, including that of self-extinction when laid down.

I am glad to have Dr. Summers's and Mr. Gilmour's assurance that no chemical addition is made to paper used in machine-made cigarettes. They admit, however, that the paper used is thicker than that employed for self-rolling. Can this be a factor of importance? Their suggestion that the disappearance of my cough resulted from my smoking less does not impress me, because that has not been the case. My financial gain rests on the fact that a cigarette which goes out when laid down, and has to be re-lit several times, gives more value for money than one which dissipates half of its substance in burning unsmoked.—I am, etc.,

Beccles, Suffolk. C. GRANTHAM-HILL.

Treatment of Cardiac Arrest

SIR,—I have been following the articles on cardiac arrest and noting the diversity of methods of dealing with it. I should like to submit the following case history, as, first, no special technique was employed and the diaphragm was not opened, and, secondly, in spite of the length of time without perceptible respiration or heart beat, the patient recovered fully, with no evidence of renal, cerebral, or myocardial damage.

Case History.—The patient, with a known duodenal ulcer of about 10 years' duration, was admitted to hospital for partial gastrectomy. Operation was commenced at 9.45 a.m., induction of anaesthesia having taken place about 20 minutes previously. The operation presented no difficulties. An antecolic Polya was performed owing to the short transverse mesocolon and an adherent wad of omental fat from an old appendicectomy which bound it down. The operation was completed at 11.45 a.m.

At 11.30 the anaesthetist expressed slight anxiety about the blood pressure, but the patient's condition was satisfactory. Dressings were applied, and as the consultant surgeon examined the specimen the patient suddenly became pulseless, livid, with dilated pupils, and respiration ceased. Auscultation of the heart was performed at 11.55 a.m., no sound being heard. The wound was opened and cardiac massage begun without opening the diaphragm. At 12 noon 2 ml. of 2% procaine hydrochloride was injected into the left ventricle, cardiac massage being carried out by the surgeon, senior registrar, and myself working continuously and in turn. At 12.08 p.m. 2 ml. of 4% procaine hydrochloride was injected intracardially and also 4 ml. of picrotoxin injected into the intravenous drip, which was continuous throughout the operation. An endotracheal tube was inserted by the anaesthetist, continuous artificial respiration being given with pure oxygen through a closed circuit.

At 12.18 I felt the first spontaneous contractions of the heart. It started in fibrillation and after a few minutes reverted to a normal beat. Phenylephrine tartrate 60 mg. was injected through the intravenous drip, and cardiac massage was continued for a further ten minutes. Massage was carried out with one hand in the wound against the apex of the heart and the left hand on the chest wall applying external pressure. The patient recovered consciousness within an hour, his only complaints being those of objections to the Tudor Edwards spectacle frames supplying oxygen and the Ryle's tube. Recovery was uneventful, although possibly a week slower than for routine gastrectomy. No manifestation of renal, cerebral, or myocardial damage was apparent. The patient has since returned to work.

As approximately 24 minutes had elapsed between cardiac arrest and the reinstitution of a heart beat, I would be glad to know if this constitutes the longest period of cardiac arrest with complete recovery.—I am, etc.,

Newton Abbot, Devon. F. COYNE.

Psychology and Psychiatry

SIR,—Dr. Albany G. Hucker (October 18, p. 880) expresses very well what may be called the official view, but he leaves out what was one of the main points of my letter (September 20, p. 669)—namely, that the general practitioner should be alerted to the importance of the psychogenic factors in the many types of ailments he is called upon to treat, and should acquire enough knowledge to recognize and advise on the domestic stresses which can cause anxiety states. The family doctor should be the first line of defence against neurosis; but when physical methods are used extensively he is apt to divest himself of responsibility and is glad to unload the patient and his troubles on to the nearest clinic.

There is a real need for a sort of half-way house between the general practitioner and the psychiatric clinic with its highly trained specialists. The importance of "paper qualifications" can easily be over-stressed. We should think not so much in terms of curing symptoms but of preventing warped personalities from developing.

I was genuinely shocked by Dr. Hucker's proposal to increase the number of psychiatric specialists by adding to the "incentives"—by which I presume he means more pay. Psychiatry is not properly a matter of choice. It is a vocation for those who have a more than ordinary interest in their fellow men, and such are apt to be indifferent to material gains.—I am, etc.,

Scarborough. R. MACDONALD LADELL.

Alcoholism

SIR,—Dr. Denys E. Howells (October 18, p. 862) is to be congratulated upon his observance of nystagmus in acute alcoholism, but I fear it will do little to make the diagnosis of the "drunk in charge" any more certain in the courts. During some experience as police surgeon prior to the National Health Service I attempted to clarify my clinical findings from the case sheets I kept. These findings showed

a certain similarity but varied from case to case, and any single finding could be upset by a good counsel. I came to the conclusion that the diagnosis was only made possible if the following factors were present: (1) the smell of alcohol; (2) the admission that alcohol had been taken; (3) the police believed the accused to be drunk; (4) that from my observation he was under the influence of alcohol or drugs.

The smell of alcohol is difficult to detect if (*a*) the accused has taken some deodorant; (*b*) the surgeon has a cold or has himself taken some drink shortly before being called to the police station. If, together with this, the accused denies taking alcohol, there is only one proof, and that is to test a sample of either urine or blood.

Briefly, and without going into percentages, the practice in other countries, or the freedom of the individual, I feel this should be made possible in all suspected cases. Why should a doctor be denied the ordinary clinical tests without which, for example, he would hesitate to label a man diabetic? The primary function of the doctor called in to see a suspected case of drunkenness should be to make as certain as he can that the symptoms presented are not due to illness.—I am, etc.,

Ormskirk. JOHN D. CRAIG.

Seasickness Remedies

SIR,—As a ship surgeon for the last few years, I have been much interested in the published opinions and tests of seasickness remedies, and note with some surprise that hyoscine is still often advised as the drug of choice for general use. You published a letter of mine in the *Journal* (February 24, 1951, p. 418) giving the opinion that hyoscine was definitely inferior to certain of the antihistamine group, and after further extensive comparison I am the more confirmed in that opinion. I have at risk every fortnight upwards of one thousand persons of all ages, travelling through two noted storm areas, the large majority of whom are not inured to regular sea travel, so that the material is very considerable.

I do not know what criteria are applied to tests of seasickness cures, but submit that the mere suppression of vomiting, and even of nausea, falls far short of the ideal. My patients are on holiday and wish to preserve every activity and interest, and to take advantage, with a hearty appetite, of a quality of cuisine rarely obtainable ashore. All this, in my experience, is better done by the antihistamines, or certain of them. I have frequent complaints by people taking proprietaries containing hyoscine, self-administered in the prescribed quantity, that these have induced a feeling of illness, whether successful in their specific purpose or not. For a year I used dimenhydrinate ("dramamine") and found more regular success with it than with hyoscine, but for the last 18 months or so I have used promethazine-8-chlorotheophyllinate ("avomine"). In my opinion it is at least as potent as dimenhydrinate, has negligible side-effects, and is happily, in these times of economic difficulty, British; it gives a higher proportion of successes than hyoscine.

I would suggest to medical men consulted on this subject that they advise early contact on board with the nursing staff, or, in known cases of marked susceptibility, with the surgeon. In most companies this is a free service. Apart from appropriate drug treatment, much help can be given by advice as to the position on board of cabin, dining-room table, and parking-place on deck or public rooms until immunity is acquired. When no such service is available, I would advise one tablet of promethazine-8-chlorotheophyllinate before rising in the morning, broken up in the mouth for two or three seconds (for quicker action), and swallowed with a mouthful of water; usually one more late in the day will suffice. For children I find antazoline ("antistin") effective; being put up in tablets of weaker dosage, the difficulty of breaking up tablets is avoided.—I am, etc.,

Sutton, Surrey. J. CRAWFORD.

POINTS FROM LETTERS

Sister Kenny

Dr. J. R. S. LAHZ (Brisbane, Queensland) writes: Mr. H. J. Seddon reviews (April 12, p. 802) Sister Kenny's book *And They Shall Walk*. . . . He says, *tout court*, "She successfully challenged the wholly illogical idea that a paralysed part must be immobilized." Where and when did Miss Kenny successfully challenge the truth that a paralysed muscle is damaged by unopposed continuous gravitational pull? This statement has possibly caused many reversibly paralysed muscles to go unsplinted and so have their weak fibres stretched and their paralyses prolonged. I find it difficult to believe that Mr. Seddon does not immobilize paralysed muscles—to some extent—and that he does not share our trust in the scientific revelation (by practice) that muscular contractures develop on the activated side of a paralysed joint more readily when the paralysed side of that joint is not kept relaxed by a splint. Mr. Seddon's statement can be taken that he does not use splints at all in the treatment of (lower motor neurone or any) paralysis. It entails a degree of heresy to which I do not think Mr. Seddon actually subscribes. That poliomyelitis cases may have been splinted too much in some instances will be readily admitted. Equally there is no doubt now that they are being splinted too little. . . . Again, when and where did Miss Kenny show that "if what is sound in her practice was universally practised to-day we should be well on the way to abolishing one of the most serious consequences of paralytic disorders—namely, deformity"? Like the other statement about the illogicality of immobilization, I can find no proof of this in the book *The Kenny Concept of Infantile Paralysis and its Treatment*, by Kenny and Pohl. There are *ex gratia* statements akin to Mr. Seddon's—but no proofs. Nor is proof to be found in Sister Kenny's earlier book *Infantile Paralysis and Cerebral Diplegia*. Will Mr. Seddon, for the benefit of medicine, please tell us of the "sound" parts of Miss Kenny's treatment which, not now embodied in accepted practice, will abolish deformity? Is it the use of hot packs, the abandonment of splintage, the adoption of an imperfect type of re-education for muscles or the avoidance of muscle charts? All paralysis clinics eagerly await a method that can be proved to avoid deformities. I shall be the first to practise such a method that has scientific backing.

Foreign Body in Arm

Dr. L. SHELDON (London, N.W.10) writes: I was consulted this morning by a female patient complaining of a painful lump 3 in. (7.5 cm.) in length and 1 in. (2.5 cm.) in width in mid right arm. She gave a history of waking up one morning, while on holiday, with a painful lump on the arm. . . . On examination, I felt what I thought was either a large splinter or needle. On careful questioning, she could not remember ever being pricked, but said that the bed had an eiderdown cover and she was sure that the lump was discovered on waking up. I referred her to hospital, where a sewing-needle 3 in. (7.5 cm.) long was removed. It is, I think, fairly obvious that this must have been in the eiderdown and that the needle must have penetrated the arm while she was asleep.

Harrow and Wealdstone Train Disaster

Mr. A. F. BROMWICH (Wembley, Middlesex) writes: I wish to endorse the experience of Edgware General Hospital (October 25, p. 942) after the recent rail crash at Harrow. Most of our cases were admitted during the first hour and had had neither morphine nor drips, and we were able to give immediate intravenous morphine as required. One patient had a plasma drip put up which had clearly run into the tissues during transit. Another patient . . . was at first diagnosed as concussion, but in actual fact was suffering from the effects of two injections of morphine. May I say, however, how impressed one was with the speed at which the injured were got out of the wreckage and removed to hospital?

Psychology and Psychiatry

Dr. W. W. MACKINLAY (Balfron, Stirlingshire) writes: As a consultant specialist to a Government department not so far in the N.H.S., I am interested in Dr. R. Macdonald Ladell's letter (September 20, p. 669). More clinics such as he suggests would undoubtedly be of help. . . . To attempt to be a psychotherapist it would appear to be essential to have: (1) "Lived" and had a wide all-round experience of life and people in general; (2) in addition to a good general medical experience to have spent an adequate period as resident physician in a mental hospital—to see the extremes of character in an attempt to gain some insight into and knowledge of character and mental processes.

Obituary

Sir TRENT CHAMPION DE CRESPIGNY, D.S.O., V.D., M.D., F.R.C.P., F.R.A.C.P.

We record with regret the death of Sir Trent Champion de Crespigny on October 27 at his home in Adelaide. He was 70 years of age.

Constantine Trent Champion de Crespigny was born at Queenscliff, Victoria, on March 5, 1882. His grandfather, a member of a family which could trace its ancestry back to the Normans, had left England to take charge as a magistrate of certain mining areas in Australia; and his father, who was Australian born, became a chief inspector of one of the leading Victorian banks. From Brighton Grammar School, Victoria, de Crespigny went on to study medicine at Melbourne University, graduating M.B., Ch.B. in 1903 and proceeding M.D. two years later. After holding resident appointments at the Royal Melbourne Hospital, he went into general practice for about two years in a country district, Glen Thompson. He then came back to Melbourne as an assistant to one of the leading practitioners in that city, but shortly afterwards he was successful in his application for the post of pathologist to the Adelaide Hospital. This post carried teaching duties, and in 1912 he was appointed lecturer in pathology to Adelaide University. He was also elected to the staff of the Royal Adelaide Hospital as a physician, and he quickly became one of the leading consultants in that city.

During the first world war de Crespigny was sent out to Lemnos with the rank of colonel to take command of the 1st Australian General Hospital. When Gallipoli was evacuated the hospital went with the Australian Army to Rouen, and he saw this move through. He was twice mentioned in dispatches and in 1917 was awarded the D.S.O. On his return to Adelaide his reputation as a clinician and as a teacher continued to grow and many honours and appointments came his way. He was appointed dean of the faculty of medicine at Adelaide University in 1928, and a year later he was elected president of the medical section of the Australasian Medical Congress at Sydney. A few years before this he had served a term as President of the South Australian Branch of the B.M.A. He became a Fellow of the Royal College of Physicians of London in 1929, and he was in addition a Foundation Fellow, member of Council, and President (1942–4) of the Royal Australasian College of Physicians. He was examiner in medicine to the universities of Sydney, Melbourne, and Adelaide. About 1935 he played a leading part in the development of the Institute of Medical and Veterinary Science of Adelaide, and he was chairman of the Institute at the time of his death. He was knighted in 1941.

Always of an adventurous disposition, de Crespigny travelled much in out-of-the-way places. He read extensively in the medical literature, and his memory for what he read was excellent. His opinion was sought by practitioners all over South Australia. In disposition he appeared to be reserved—he was a very tall man and spoke with a slow drawl—but he was full of dry humour, and as his friends learnt to know him they came to appreciate more and more his very high qualities.

He was twice married. His first wife, who was the daughter of the late E. W. Hughes of Melbourne, died in 1943. There were two sons (one is now in practice in Adelaide) and two daughters of this marriage. In 1945 he married Mary, daughter of W. C. Jolley, of Wentworth, N.S.W., and they had one daughter.

J. A. DRAKE, M.D., F.R.C.P.

Dr. John Alexander Drake, who died in King's College Hospital on October 29 at the age of 73, was born at Clifton, Bristol, on November 4, 1878, and was educated at Malvern College. He studied medicine at King's College, and while there he entered fully into the college activities and yet found time to win such distinctions as the Warneford Scholarship and the Sambrooke Exhibition, as well as other prizes. After qualifying M.R.C.S., L.R.C.P. in 1902 he became house-surgeon to the late Sir Watson Cheyne, and he had, therefore, a direct link with Lord Lister's work. He took the London M.B. in 1903, and two years later he entered general practice at Tenby, Pembrokeshire, a decision taken in the hope that his health, which was not very good at the time, would benefit in the climate of S.W. Wales. In 1915, however, he was still unfit for military service, but he did succeed in joining the 4th London General Hospital as a civilian physician in charge of the medical division. His interest in skin diseases was then allowed further scope, and he frequently attended the clinics at King's College Hospital, which were then in the charge of the late Professor Arthur Whitfield.

At the end of the war Drake's association with King's College Hospital was strengthened, for after service as a clinical assistant he was appointed to the honorary staff of the hospital in 1920 as assistant physician in the dermatological department and director of the venereal diseases department, where he succeeded the late Dr. W. d'Este Emery. He took the D.P.H. in 1919, and in the following year he proceeded M.D. and became a Member of the Royal College of Physicians. In 1927, the year after he was elected F.R.C.P., he became physician in charge of the dermatological department at King's, and he continued to hold the post until his retirement from the active staff of the hospital in 1937, when he was appointed consulting physician to the hospital and emeritus lecturer to the medical school. He served for a time as secretary of the Section of Dermatology of the Royal Society of Medicine, as assistant editor of the *British Journal of Dermatology and Syphilis*, and as examiner in medicine to the Conjoint Board. His main interest, however, lay in his own hospital and perhaps even more particularly in the medical school, of which he was appointed sub-dean in 1920 and vice-dean two years later. He became dean in 1932, on the retirement of Mr. H. Willoughby Lyle. The fact that Drake held these appointments over such a long period is in itself a sufficient indication not only of his popularity with the students but also of the trust placed in him by his colleagues. His chronic ill-health had never hardened his character, and his quiet voice and friendly smile will be long remembered. In 1908 he married Lorna, the daughter of Charles James Stewart, to whom the sympathy of his many friends is extended.—M. S. T.

P. H. MITCHINER, C.B., C.B.E., M.D., M.S., F.R.C.S.

We are indebted to Lieutenant-General FREDERICK HARRIS, Director-General of the Army Medical Services, for the following appreciation of the late Major-

General P. H. Mitchiner, whose obituary notice was published in the *Journal* of October 25 (p. 943):

The great services of Major-General P. H. Mitchiner to the Territorial Army, both before and during the war, have already been outlined in the *Journal*, and I should like to endorse all that has been said. Nevertheless, I feel that it is appropriate that I, as Director-General Army Medical Services, should add my personal tribute to a great and loyal officer of the R.A.M.C.

I first met Major-General Mitchiner, then Colonel Mitchiner, in October, 1934, when, together with a number of Territorial medical officers, I attended a week-end training exercise at Brighton. I had gone as a regular R.A.M.C. officer to help the Territorial medical officers with their training, but I very soon found that Colonel Mitchiner and the officers trained by him knew at least as much about the tactical handling of field medical units as I did. From that day he and I became friends, and latterly close friends, and a wonderful friend he was, not only to me but to the whole of the R.A.M.C., both Regular and Territorial. From the end of the war until his death he was, as adviser to the D.G.A.M.S., his right-hand man on all matters concerning the T.A. medical service. In this responsible task he was of the very greatest help, and his wide knowledge of the Territorial Army, and indeed, it seemed, of every officer in it, was invaluable. His grasp of training problems was remarkable: his comments were always candid and outspoken, but mellowed by wit and a sense of fun. He never spared himself, and during the last few years, although his health was far from good, he visited during the training season numerous T.A. units throughout the United Kingdom, giving advice to the officers in command and taking part in their social activities. The present high standard of training of the T.A. medical services is in large measure due to his enthusiasm, knowledge, and personality. At the annual training exercise held this year by me at Mytchett, near Aldershot, a large number of R.A.M.C. officers—Regular, Supplementary Reserve, and Territorial—attended, and "Mitch," as he was affectionately known to us all, was among those invited. Owing to ill-health, however, he was unable to attend. At the opening session of the exercise it was decided to send him a telegram saying how much he was missed, and wishing him a speedy recovery. This telegram he received only a day or so before his death, and I am glad to know that it pleased him greatly. There is no doubt that "Mitch" was a very great and lovable personality who will be missed by the whole of the Army. We shall not soon see his like again.

W. A. B. writes: May I, who 17 years ago was one of Philip Mitchiner's very junior officers in the R.A.M.C. (T.A.), pay a tribute to his memory? One felt a sense of shock, almost of unbelief, at the news that "Mitch" had passed over. It seemed that his love of life, his impish sense of humour, and his devotion to his surgical craft and to his country should have continued for many years to come. It is poor comfort for those who had the privilege of his confidences that the suddenness of his death is what he would have wished. His professional attainments need no pen of mine: they have already been described. But it was the man himself that mattered: the "brass hat" (whose picturesque language contained neither venom nor spite) who was so kindly and so helpful to his junior officers in the difficult years of Territorial Army expansion; who half an hour before he was due at a T.A. camp ("The A.D.M.S. is coming round!") would wander in, unescorted, in drizzling rain, and amble deep in mud round the lines, chatting amiably and understandingly to all and sundry; who would then come in later, as an honoured mess guest, with an avuncular benignity which concealed the keen brain and the succinct summing-up of both senior and junior officers; and who could cross swords with captain-quartermasters, in all friendliness, on the intricacies of the G.1098. The humanity of him, the selfless dedication of service to his country for 40 years, the shaven head, the mobile humorous mouth from which a smile was never far away, the triple row of ribbons—all are gone, and the T.A. will miss him and mourn him.

Fifty years in general practice in the same town is a record which few doctors attain, but Dr. RICHARD COFFEY, who died on September 6 at the age of 78, was one of the few. Born on October 2, 1873, he was educated in Dublin and qualified L.R.C.P.&S.I. in 1894, and joined his uncle in practice at Barrow-in-Furness at the beginning of the century. He continued to attend his patients up to a few weeks before his death, although for the last three years he was much handicapped in his movements by a leg injury. Dr. Coffey served throughout the war of 1914–18 in field hospitals in France, attaining the rank of major and winning the D.S.O. in 1918. He had had a long association with the Territorial Army, and for his services he was awarded the Territorial Decoration in 1925. Though conducting a busy practice, he found time for many other activities, particularly yachting. His kindly, cheerful personality will be much missed by his colleagues and patients.

Dr. N. C. WALLIS, who died at Perranporth, Cornwall, on September 20 at the age of 72, practised for many years in Norfolk. Neville Courtenay Wallis was born on January 3, 1880, and received his medical education at the London Hospital, qualifying L.M.S.S.A. in 1908. He became interested in anaesthesia and was appointed honorary anaesthetist to Charing Cross Hospital and the London Lock Hospitals. During the war of 1914–18 he served as anaesthetist to No. 1 Stationary Hospital in France and to No. 1 British General Hospital in Mesopotamia. After the war he settled in general practice at Stalham, in Norfolk, becoming also medical officer in charge of the hospital at Ingham and medical officer and public vaccinator for the Stalham district. He retired from practice in 1945 and went to live at Perranporth.

D. F. R. writes: I knew Neville Wallis, as a friend and as a patient, only during the last years of his life, after he had retired to Cornwall crippled by polyarthritis and no longer able to cope with his practice. I know that his life at Stalham had been a full one, embracing many social, political, and sporting activities. He had been chairman of the parish council for a long period, and he was a loyal, enthusiastic, and eminent freemason, a good yachtsman, and a good shot. He was a general practitioner of the older school, self-reliant, capable and energetic, astute at improvisation, and above all always thoughtful of the welfare of his patients. As a friend he was a wonderful character, always interested in life in his new surroundings and in medical activities generally. One turned to him with equal eagerness for an idle chat or for advice. As a patient he was among those rare people who make a doctor's life really worth while and on whom it is a true privilege to attend. For the last five or six years of his life his arthritis was so devastating that there were very few joints in his body which he could move, and those only with great pain. A cigarette or a spoon had to be placed between his lips, for his hands could not reach them. Yet never once did I or my partner hear him complain, and when one was allowed to do any small thing to ease his lot one had first to accept his apologies for any trouble he might be causing. I learned many things from Neville Wallis, not the least of which is that it is possible to live with pain as your constant companion and to overcome it. For him death came indeed as a merciful release from suffering, but all those who knew him loved him, and they will miss him for a long time to come.

Dr. G. P. HENDERSON, who died at Bideford on September 29, after a long and painful illness, was born at Redcar on July 15, 1874. Of mixed Yorkshire and Scottish descent, his family had close connexions with the countryside and the sea, for both of which he retained a love. George

Pouncey Henderson was educated privately in Cumberland and at the University of Edinburgh, where he graduated M.B., C.M. in 1895, proceeding M.D. in 1900. After a period as a ship surgeon he settled in general practice at Stockport, where he remained for 35 years. He was honorary surgeon to the Stockport Infirmary, and after his retirement in 1937 he was appointed consulting surgeon. In spite of the leisure it gave him to pursue his hobby of trout-fishing, retirement to Bideford proved irksome, so during the last war he returned to practice, assisting hard-pressed local practitioners. Eventually failing health forced him to relinquish his work and, at the same time, his long walks in the country, from which he had always drawn so much strength.

E. M. B. writes: The life and character of Dr. Henderson epitomized that which was finest in the great English and Scottish medical tradition. He was the ideal family physician, dignified, skilful, wise, discreet, and always kind. Trained to his craft by great teachers in a day when medicine was less highly specialized, he was a physician of judgment and dexterity, and he was equally at home in operating theatre and cottage. He held the universal trust and admiration of his patients and his colleagues alike. Like many men who have spent long periods at sea, he always knew "what to do" both in medicine and in life. Of high integrity and, concerning personal manners and morals, fastidious to a degree, he was the trusted and wise adviser to many families. He always had sympathy and help for those in trouble, whether or not of their own making. His manner was modest, his humour mildly ironic, his own philosophy stoic, but he never hid his real affection for young people, who delighted in his company. In writing of my old friend I have tried to recall to memory a generation of practitioners of which he was a perfect example. Perhaps the best epitaph for him, and them, is, in his own words, "It is a doctor's duty to do his best, and he should be trained and should train himself to know how to do it."

By the sudden death of Dr. JAMES AITKEN at his home on October 2 at the age of 61 the residents at Stanmore, Middlesex, have lost a medical practitioner who was greatly loved and respected. He was born on July 20, 1891, and was educated at the University of Edinburgh, where he graduated M.B., Ch.B., with honours, in 1917. After holding a number of hospital appointments he entered the R.A.M.C., and served with distinction in many theatres of the war of 1914–18. After demobilization he practised for a time at Liverpool and at Finchley, in North London, before finally settling at Stanmore, where in a very short time he acquired an excellent reputation among his patients. He was superintendent of the local cottage hospital and one of its trustees, and under his guidance the hospital saw its best years. It was a bitter blow to him when the introduction of the National Health Service caused the hospital to be converted into a home for the chronic sick, and he felt a great sense of personal loss thereafter. During the last war he served in the R.A.F., and rose to the rank of wing commander. Dr. Aitken's qualities as a general practitioner were of the highest, and his death will be mourned by many, for he was entrenched deeply in the affections of all who came into contact with him professionally or socially. He leaves a widow and one daughter.—S. H.

Dr. FREDERICK JAMES LAWSON, who died in London on October 8 at the age of 75, was born on October 13, 1876, the son of Mr. James Lawson, of Hassocks, Sussex, and was educated at University College and at University College Hospital, London, qualifying M.R.C.S., L.R.C.P. in 1901. Two years later he took the degree of M.B. of the University of London. After holding house appointments at University College Hospital, he settled in general practice at South Kensington, becoming also anaesthetist to the Royal Cancer Hospital and to the Gordon Hospital for Diseases of the Rectum. He was surgeon to the B Division of the Metropolitan Police from 1912 to 1942. He served in the R.A.M.C. in the war of 1914–18 in Salonika. Dr. Lawson was an excellent type of the now nearly extinct general practitioner with specialist leanings, and was a man of high repute among his colleagues for dependability, resource, and good-neighbourliness. He married Miss Ethel Frances New, daughter of Dr. G. W. New, and she survives him, with one daughter.

Dr. JOHN JOSEPH FITZGERALD, a psychiatrist who had outlived almost all of his contemporaries, died at Shenley, Hertfordshire, on October 15 in his 84th year. He qualified L.R.C.P., L.R.C.S.Ed. in 1894, and obtained the M.D. (Brussels) in 1898, thereafter taking the L.R.C.P.I. in 1903 and the M.D.(Durham) in 1911. He entered the Irish mental hospital service in 1896, and worked at the Cork Mental Hospital for over 40 years. Dr. FitzGerald long preceded most of his Irish colleagues in realizing the value of psychotherapy; in the early nineteen-twenties he conducted in his home at Cork what is believed to have been the first psychiatric out-patient clinic in Ireland. His wife, Dr. Lucia FitzGerald, joined him in that enterprise, and in 1926 they published in the *Journal of Mental Science* a record of the psychiatric treatment of out-patients. He was well known at one time to the students of the University of Cork as a lecturer in mental diseases, but the best tribute to his teaching ability lies in the fact that his son and his two daughters and their husbands have all followed him in specializing in psychiatry, so that he enjoyed the probably unique position of having an all-psychiatrist family. Dr. FitzGerald had also earned a reputation as an antiquarian and genealogist, and up to the time of his death was a member of the Royal Society of Antiquaries of Ireland. He was a former president of the Munster Branch of the British Medical Association, of which he had been a member for many years.

We record with regret the death of Dr. J. J. O'B. LAVERY at Glasgow on October 19 at the age of 30 after a long illness. James Joseph O'Brien Lavery was born on March 15, 1922, the son of the late Dr. William Lavery, and he took his medical training in Glasgow, qualifying in 1949.

P. G. McG. writes: Dr. Jimmy Lavery's medical studies had been interrupted by his father's death and his own ill-health, but with the persistence and enthusiasm which were characteristic of him he qualified in 1949. He was not able to practise energetically or for long his chosen profession, and soon after qualifying had to resign himself to a purely academic interest in medicine. With real keenness he kept up with the literature, and loved to talk shop with his more fortunate friends and colleagues. His insight into his own condition did not in the slightest diminish his enthusiasm, cheerfulness, and human sympathy. Had he lived, those qualities would have made him a great doctor.

Dr. FRANK LESLIE THOMAS, a well-known general practitioner in North Devon, died on October 19 at the age of 74. He was born in Woodford, Essex, and studied medicine at Guy's Hospital, qualifying in 1903. Among the hospital posts he held were those of senior house-surgeon at the Royal Devon and East Cornwall Hospital, house-physician at the East London Hospital for Sick Children, and obstetric resident at Guy's. He went into general practice at Barnstaple, where he worked for the rest of his professional life, except for a period of service in the R.A.M.C. during the first world war, during which he was for a time in Mesopotamia. On his return he was appointed honorary surgeon to the North Devon Infirmary (retiring in 1942 as honorary consulting surgeon) and medical officer in charge of the Barnstaple public assistance institution. An active member of the B.M.A., he was chairman on three occasions of the Barnstaple Division and president of the South-western Branch in 1939, an office which he held until the end of the war. He was also interested in local public life, and was elected mayor of Barnstaple in 1922. His happy, genial personality, his unswerving loyalty, and his kindliness were the features of the charming character his colleagues and friends knew as "Tommy."—M. K.-L.

Medical Notes in Parliament

Intern Year

In the House of Lords on October 28 LORD ONSLOW moved that the Medical Act, 1950 (Period of Employment as House Officers), Regulations Approval Order of Council, 1952, be approved. He said the object was to carry out the duty laid upon the G.M.C. under the Medical Act, 1950, that it should prescribe a period of free registration service for doctors before they went into practice. It was originally intended to prescribe a period of 12 months in the Bill itself, but by amendment this duty was left to the G.M.C., which had decided on 12 months as the period for which medical students should work in hospitals as house-officers before they were finally registered and went into general practice.

LORD WEBB-JOHNSON said there had been anxiety lest the resolution was introduced before there was an assurance that the necessary posts would be available. After graduating, a medical student could only secure provisional registration when he succeeded in getting an appointment which would enable him to obtain the necessary 12 months' experience entitling him to permanent registration. These men or women should not drift, but be posted without delay to appointments which would give the experience they required.

LORD ONSLOW said that arrangements had been made to meet this point. A man would start to make his arrangements for a post when he expected to qualify in the hope that he would in fact succeed in qualifying. The G.M.C. published a list of approved house posts which he was told gave every opportunity for the person concerned to find an adequate position when he qualified.

LORD HADEN-GUEST said the bulk of those concerned with medical administration regarded this procedure as a definite advance which would improve the status of the profession. It would be good for the profession and very good for young men starting their career.

The House then agreed to the Motion.

DEBATE ON DANCKWERTS AWARD

Mr. H. MARQUAND on October 30 drew attention to the report of the Working Party on the distribution of remuneration among general practitioners. He said the first three years of experience of the National Health Service had revealed defects in the working of the general-practitioner service. Practitioners themselves complained from time to time about the large number of patients whom some of them were asked to look after. Some suggested they had insufficient opportunities for hospital practice or insufficient access to modern diagnostic aids. Younger men among them complained bitterly of the difficulties they found in entering practice as principals. Patients expressed disappointment at the waiting in surgeries and at the slowness of development of the National Health Service. Ministers too had their complaints, especially at the size of the drug bill. The general public sometimes forgot that the rate of remuneration of general practitioners covered their expenses as well as their earnings. About £4 out of every £10 received went in essential expenses. If a global sum had to be shared out the fewer there were to share it the better chance an individual had of obtaining a satisfactory income. Such a system laid itself open to the danger of restriction of entries.

He could not but be worried at the growth in the number of salaried assistants. In 1948 there were 17,438 principals and 562 salaried assistants working for them. In 1951 there were 18,195 principals and 1,724 assistants. The principals had increased by about 4%, the assistants by 206%. These assistants included men and women who had returned from the Forces or from the Colonial Service, and there were some very hard cases among them.

Surprised at Result

Mr. Justice Danckwerts had found in favour of the claim by the doctors. Mr. Marquand said he was surprised, and said so at the time, by the extent to which Mr. Justice Danckwerts found the claim proved that the central pool had not been large enough. However, having resorted to an independent opinion there was no sense in complaining when that opinion went against one. The back money granted in the Danckwerts adjudication was in course of being paid, and Mr. Marquand thought there was no need to discuss it. The second part of the bargain remained. If so large an amount of money was to be made available the chances of the Working Party getting a really satisfactory improvement in the Service and all the other things laid down in the agreement were much improved. But when his friends read the report of the Working Party they issued a statement on June 24 that a great opportunity had been missed. The Fellowship for Freedom in Medicine issued a statement in which they said that the opportunity had not been fully grasped. It was significant that Lord Horder and his organization, studying the report of the Working Party, came to the same conclusion as Mr. Marquand and others on the Opposition side of the House.

Cutting Lists

The first term of reference for the Working Party was to discourage unduly large lists. The Working Party proposed to reduce the maximum list from 4,000 to 3,500. It remained true that 3,500 patients was a large number for a doctor to look after. Even although as a first step a greater reduction could not be made in the maximum figure, provision should have been made for tapering off the capitation fee between 3,000 and 3,500 patients to give less inducement to obtain the maximum number. He asked the House to consider the problem of the small-list doctors. The greatest intensity of complaint against the Working Party's report had come from these.

The *British Medical Journal* of August 9 (p. 327) had said, presumably reporting something agreed on with Mr. Macleod, that a sum of £50,000 would be set aside annually to help elderly doctors. If other categories of doctors, especially those with small lists, turned out to have lost under the new arrangements something could be done to help them when the final settlement for the year was made. A substantial sum of money was likely to be available for this. Mr. Marquand asked how substantial the sum would be and how the doctors would have to apply for it. Would it be on the basis of a means test? Might it not be provided now to meet the grievance of the small-list doctors by an increase in the capitation fee, say between £250 and £500?

Assistants and Partners

The third term of reference to the Working Party had been to make it easier for new doctors to enter practice. To-day salaried assistants numbered 2,300, and in addition 500 hospital registrars sought employment. It was reasonable that a young doctor should begin that way, but a man should not be an assistant year after year and be given a number of patients in respect of whom he knew his principal drew much more money in fees than he paid his assistant in salary. The Working Party had found a useful way of encouraging practitioners to take partners rather than assistants by proposing a special loading and by saying this loading would not apply in the case of patients attributed to an assistant. None the less, grave misgiving had been aroused among unestablished doctors by the use of the term "permanent assistant" in paragraph 5. A safeguard was also needed against the possibility of establishing unfair partnerships. This could be done by agreement without amendment of the Working Party's report. The British Medical Association supplied model contracts for employment of assistants. Mr. Marquand wondered whether it could be persuaded to draw up a model contract for partnerships.

The fourth term of reference of the Working Party had been to stimulate group practice. The obstacle to the extension of health centres, which were the ideal way of carrying out group practice, was finance, and he did not suggest that any money in the central pool should be used for building health centres. Yet the report of the Working Party devoted only one paragraph of five lines to the subject and said that a sum of money—provisionally £100,000—should be set aside so that it might be possible if necessary to introduce further measures to stimulate the formation of partnerships working as a group practice. That did not sound like stimulation to Mr. Marquand. He remarked that he had tried in what he had said to avoid exciting party feeling. Though he had been severely criticized in the *British Medical Journal* for raising the matter at all he had refrained from criticism of the British Medical Association.

Encouraging G.P.s

Mr. SOMERVILLE HASTINGS said he had no quarrel with the Danckwerts award. He did not think it too much. Unless the status of the general practitioner was raised the best men in the profession would not go into general practice. His quarrel was not with the Danckwerts award but with the Working Party's report. That report did not raise sufficiently the status of the general practitioner. Mr. Hastings said he did not look at the size of a doctor's list when he wished to know his quality. He asked the medical superintendent of the nearest hospital what sort of cases the doctor sent to that hospital and whether they had been kept waiting too long before they were recognized and dealt with. In the consultant service there were merit awards. More should be done to provide special rewards at the top of the general-practitioner service to which any young man or woman could look forward if he or she had special ability and capacity. Mr. Hastings wished to see much more done to discourage permanent assistantships. Much more should be done to stimulate partnerships, and to get doctors to work together in partnership would be a first stage of development of health centres.

Mr. ANGUS MAUDE found it difficult to see how the Working Party could go far beyond what it had done. Its report had been produced in a hurry, and he thought there was justice in the complaint of some doctors that they had been asked to accept it in too much of a hurry.

Dr. BARNET STROSS said it was a mistake to limit the sum awarded to group practice to £100,000 or to give it as a free gift in small sums. The sum should be at least £500,000, not awarded as gifts but in the form of loans at a low rate of interest for 10, 15, or 20 years. Under the conclusions of the Working Party the taxpayer was not likely to obtain great immediate benefit, except that there might be better distribution of doctors and some curtailment of excessive lists. The Labour Party desired more than that. It asked the Minister to intervene particularly for better accommodation for the public in surgeries and waiting-rooms.

Minister's Reply

Mr. I. MACLEOD said nothing had been heard that day in disapproval of the theory of loading or weighting, although suggestions had been made that another method should be chosen. Mr. Marquand, in a letter to the *British Medical Journal* on August 9, had said that the Socialist Party sought an improvement in the general medical service within the Health Service rather than party advantage. Mr. Macleod said he agreed with the first part of the sentence but took the second with a small piece of salt. The size of the ideal list could not be settled by rule of thumb. He deplored the attacks which had been made in the columns of professional journals against the big-list man. He was delighted that such attacks had not been made that day. The big-list man would suffer a considerable decrease of income next year compared with this year. His ordinary percentage increase after the scheme in comparison with pre-scheme would be a great deal less than in the case of a man in the middle part of the list. He had read in the *British Medical Journal* and elsewhere ill-tempered arguments against what had been achieved by the Working Party made on the assumption that it was a term of reference of the Working Party to help those with a small list. The terms of reference did not say that. Mr. Marquand did not mean that. The important part of the terms of reference was: "To bring about a relative improvement in the position of those practitioners least favourably placed under the present plan of distribution."

Most people who had studied the problem would probably claim that the people least favourably placed were not only those with small lists but more particularly those with medium-sized lists who were not in industrial areas and perhaps previously had a measure of private practice. A leading article in the *British Medical Journal* of September 27 (p. 709) had said the Working Party tried to help the unestablished practitioner and gave the greatest encouragement to a middle group with lists of average size.

Mr. Marquand had told the profession categorically that the people to whom he thought special reference should be made were those with lists of the order of 1,000 to 2,500. Accepting the fact that the Working Party looked, as he knew they had done, to the middle groups first, Mr. Macleod said the terms of reference were implemented. The largest percentage increases were those with the 1,500 list, with an increase of 42.6. The award tapered off both upwards and downwards from that figure, so there had been a relative, not just an overall, improvement in the position of these groups. It had been suggested that the Government should load the first 1,000 or some suitable figure. That also, though not so obviously, was inconsistent with the terms of reference. It would mean that a smaller loading would have to be made and it would tend to perpetuate maldistribution of doctors. It would make it more difficult for the Ministry of Health to get doctors in designated areas, where they must be for a very good Service.

2,000,000 to Change Doctor

Every calculation he had seen about the effect of these new proposals forgot that up to 2,000,000 patients would have, either under the notional list agreements or by changing their doctor, to find another doctor. That was bound to make it easier, particularly in the designated areas, for small-list doctors to increase their practices or to be taken into partnership by someone who already had a big list. He hoped younger doctors would not assume that because they had small lists now they would always have small lists, and that it was the duty of the State to subsidize them for ever. Frankly he did not intend to take competition out of medical practice. The Government should try to match rewards with effort and achievement. It was not, and never had been, part of the policy of the Government to have a salaried service in the medical profession. Hardship cases would exist, although their numbers were considerably smaller than some members had suggested. A sum of £50,000 was to be set aside to deal with cases of hardship as yet unspecified. In addition there was the rider passed at the meeting of the profession that an appropriate portion of the final settlement moneys should be put aside to remedy any particular difficulties.

It seemed to him beyond dispute that the initial practice allowance was an improvement in the fixed annual payment. The I.P.A. produced £1,250 plus full basic capitation fee in three years. The fixed annual payment produced £900 plus capitation fees reduced by one-seventh. That was an important inducement. A second inducement was the reduction in the maximum lists, which was bound to help, particularly in heavily populated areas. He detected some apprehension among doctors about how the notional system was to work. He recognized dangers of abuse in it. There were dangers of straw partnerships being set up solely to get the value of loading of additional numbers of partners' lists. The Ministry was watching this matter very closely with the executive councils, on whom the main burden must lie for deciding whether there was a genuine partnership or not.

Stimulating Partnerships

Lastly came the question of assistants. Mr. Macleod said the term "permanent assistant" used in para. 5 of the Working Party's report had no sinister meaning. It had been used ever since the 1948 regulations to describe the type of doctor whom a practitioner was permitted by the executive council permanently to employ as an assistant. The number which a doctor was entitled to count had been reduced from 2,400 to 2,000, which made it less attractive to employ an assistant. More important was the fact that these 2,000 did not qualify for loading. There was therefore a considerable inducement for a principal with a big list to end an assistantship and take the young man or woman into partnership. Mr. Macleod hoped this would happen. He agreed with all that had been said about not wanting an interminable period of assistantship. It would be premature as yet to take further steps perhaps limiting the length of time a man could employ an assistant, but the Ministry would particularly watch the point as the scheme went forward from April next year.

The Working Party had reached agreement within its own meeting, the proposals had been put before a series of local meetings, and finally before a conference of the profession. They had been approved by the conference and later by the representative bodies. He had heard that day a suggestion echoed that some form of pressure had been brought to bear on those meetings. He did not attempt to speak for the profession, but did not believe a single doctor could have thought that the Government, because of a criticism of the Working Party, would run away from implementation of the Danckwerts award. He noted that a letter in the *British Medical Journal* had said the scheme had been approved by the Assistants and Young Practitioners Subcommittee and no rider had been put forward to say the approval was merely a preference for the loading between 500 and 1,500 as against a higher figure. Mr. Macleod said it was his view that the scheme could go forward as it stood.

Poisonous Substances in Agriculture

The Agriculture (Poisonous Substances) Bill was taken in Committee on October 27. In Clause 1 (Protection of Employees against risk of Poisoning) Mr. A. J. CHAMPION moved an amendment to provide for medical examination before men should be called upon to carry out the class of work mentioned in the Bill and that provision should be made for periodic re-examination. His party also wished the Bill to make specific provision for regular medical examinations where at present it only empowered the Minister to make regulations for the purpose. The trade unions concerned had suggested examinations at weekly intervals and the suspension of workers who showed early toxic symptoms.

Mr. NUGENT, Joint Parliamentary Secretary for Agriculture, said the Bill gave the Minister the specific powers for which Mr. Champion asked. A voluntary scheme had been operated by the Ministry this year and the Ministry had observers out in the field to see how it worked in practice. This voluntary scheme would be the basis of the first set of regulations.

The amendment was withdrawn. On a later amendment, Mr. Nugent explained that power of entry into dwelling houses proposed to be conferred on inspectors of the Ministry was for examination for records showing how many hours of work each man had spent with these poisonous sprays.

The Committee Stage then closed and the Bill was read a third time. The Royal Assent was signified on October 30.

The New Session

The Speech from the Throne with which the Queen opened Parliament on November 4 announced that proposals would be made for improving the maternity benefits under the National Insurance Scheme, and also for the further amendment of the National Insurance (Industrial Injuries) Act.

INFECTIOUS DISEASES AND VITAL STATISTICS

Summary for British Isles for week ending **October 18** (No. 42) and corresponding week 1951.

Figures of *cases* are for the countries shown and London administrative county. Figures of *deaths* and *births* are for the 160 great towns in England and Wales (London included), London administrative county, the 17 principal towns in Scotland, the 10 principal towns in Northern Ireland and the 14 principal towns in Eire.

A blank space denotes disease not notifiable or no return available.

The table is based on information supplied by the Registrars-General of England and Wales, Scotland, N. Ireland, and Eire, the Ministry of Health and Local Government of N. Ireland, and the Department of Health of Eire.

CASES in Countries and London	1952					1951				
	Eng. & Wales	Lond.	Scot.	N. Ire.	Eire	Eng. & Wales	Lond.	Scot.	N. Ire.	Eire
Diphtheria	29	1	16	1	1	33	3	12	0	1
Dysentery	181	15	102	6	0	162	38	48	2	1
Encephalitis, acute	2	2	1	0		5	0	0	0	
Enteric fever:										
Typhoid	6	2	2	1		3	0	0	0	0
Paratyphoid	15	0	1 (B)	0		81	0	1 (B)	0	1 (B)
Food-poisoning	114	9		0		88	6		0	
Infective enteritis or diarrhoea under 2 years				13	20				16	41
Measles*	7,785	964	129	61	12	1,809	71	100	135	156
Meningococcal infection	30	0	12	1	1	36	3	17	1	2
Ophthalmia neonatorum	29	5	9	0		41	5	11	1	2
Pneumonia†	439	23	224	1		424	18	162	1	
Poliomyelitis, acute:										
Paralytic	86	2	5	4	0	67	0	19	5	4
Non-paralytic	33	5				52	2			
Puerperal fever§	254	26	16	0		245	33	16	2	
Scarlet fever	1,760	171	331	26	61	1,135	84	260	32	43
Tuberculosis:										
Respiratory			135	21				151	34	
Non-respiratory			22	8				24	5	
Whooping-cough	1,074	63	111	35	33	1,516	85	317	37	72

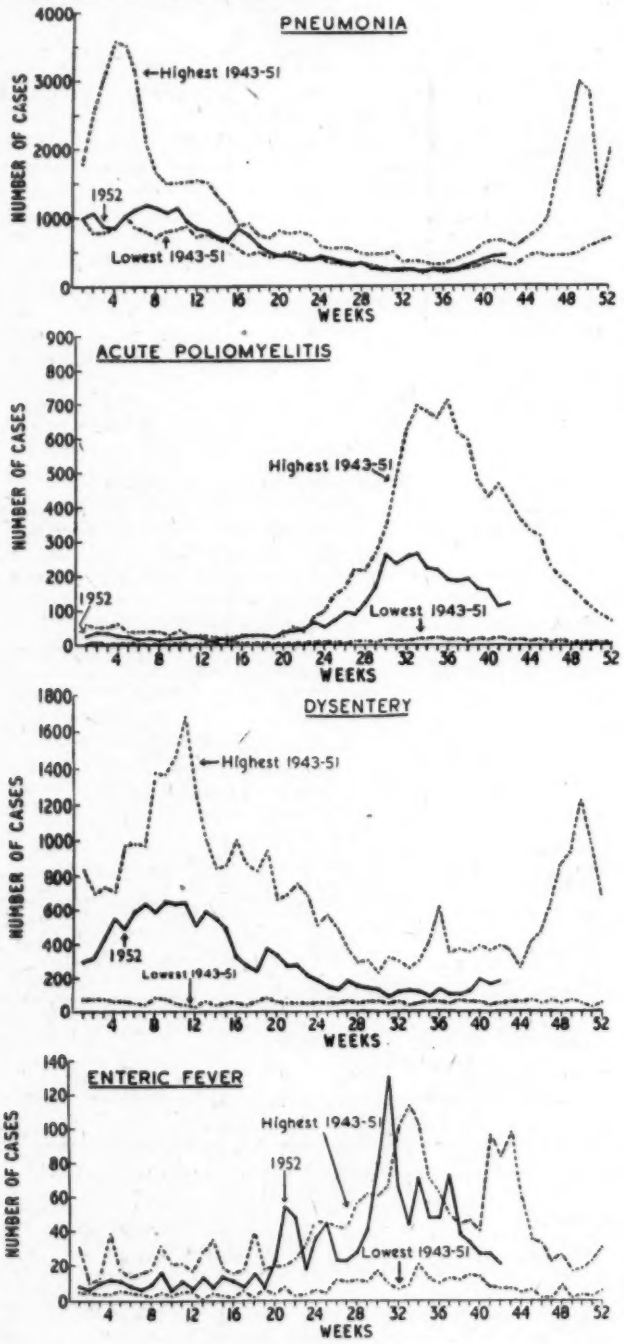
DEATHS in Great Towns	1952					1951				
	Eng. & Wales	Lond.	Scot.	N. Ire.	Eire	Eng. & Wales	Lond.	Scot.	N. Ire.	Eire
Diphtheria	1	0	1	0	0	*1*	0	*0*	0	0
Dysentery	0	0		0			0		0	
Encephalitis, acute		0			0		0			0
Enteric fever	0	0		0		*0*	0	*0*	0	0
Infective enteritis or diarrhoea under 2 years	7	0	1	0	1	*5*		*4*	0	1
Influenza	11	1	1	0	1	*18*	2	*1*	0	0
Measles		0		0	0		0	*0*	0	0
Meningococcal infection		1					0	*0*		
Pneumonia	173	25		16	7	*151*	25		7	12
Poliomyelitis, acute	2	0			0	*3*	0			0
Scarlet fever		0		0	0		0	*0*	0	0
Tuberculosis:										
Respiratory	104	9	19	4	6	*158*	29	*17*	2	3
Non-respiratory		5	1	0	3		3	*2*	0	2
Whooping-cough	1	0		0	0	*0*	0	*1*	0	1
Deaths 0–1 year	176	16	25	11	9	*176*	23	*25*	14	19
Deaths (excluding stillbirths)	4,951	702	556	133	169	*4,450*	704	*510*	107	146
LIVE BIRTHS	7,323	1029	920	220	392	*6,340*	1060	*807*	198	380
STILLBIRTHS	209	23	20			*171*	33	*12*		

* Measles not notifiable in Scotland, whence returns are approximate.
† Includes primary and influenzal pneumonia.
§ Includes puerperal pyrexia.

Vital Statistics

Graphs of Infectious Diseases

The graphs below show the uncorrected numbers of cases of certain diseases notified weekly in England and Wales. Highest and lowest figures reported in each week during the nine years 1943–51 are shown thus - - - - - - -, the figures for 1952 thus ————. Except for the curves showing notifications in 1952, the graphs were prepared at the Department of Medical Statistics and Epidemiology, London School of Hygiene and Tropical Medicine.



Infectious Diseases

The only large fluctuations in the incidence of infectious diseases in England and Wales during the week ending October 18 were a rise of 2,069 in the number of notifications of measles, from 5,716 to 7,785, and a rise of 143 in scarlet fever, from 1,617 to 1,760.

The notifications of measles have risen continuously for five weeks, and the number is now treble that of five weeks earlier. During the week reviewed the largest rises in the incidence of measles were 302 in Essex, from 335 to 637; 282 in London, from 682 to 964; 159 in Suffolk, from 135 to 294; and 137 in Yorkshire West Riding, from 621 to 758. Only small changes occurred in the local trends of scarlet fever. The number of notifications of whooping-cough, 1,074, was 4 less than in the preceding week. 29 cases of diphtheria were notified, an increase of 5 on the total of the preceding week. The chief features of the returns of diphtheria during the week were a decrease of 5 in Yorkshire North Riding, from 6 to 1, and rises in Lancashire from 2 to 9, and in Warwickshire from 0 to 4. The largest centres of infection were Birmingham C.B. 4 and Manchester C.B. 4.

Notifications of paratyphoid fever fell from 25 to 15. Of these cases, 11 were notified in Wales (Monmouthshire 6, Glamorganshire 4, Carmarthenshire 1). All the cases in Monmouthshire were notified in Tredegar U.D.

Notifications of acute poliomyelitis increased by 10 from 109 to 119. The notifications were 6 fewer for paralytic and 16 more for non-paralytic cases than in the preceding week. The largest returns were Surrey 17 (Guildford M.B. 8), Middlesex 11, and Essex 9 (Southend-on-Sea C.B. 6).

The notifications of dysentery, 181, were 21 more than in the preceding week. The largest centres of infection were Lancashire 61 (Blackburn R.D. 13, Liverpool C.B. 12, Ormskirk U.D. 12, Manchester C.B. 9), Yorkshire West Riding 26 (Leeds C.B. 18), London 15, and Essex 13 (Wanstead and Woodford M.B. 9).

The largest outbreak of food-poisoning notified during the week was 33 cases in Lancashire, Stretford M.B.

Week Ending October 25

The notifications of infectious diseases in England and Wales during the week included scarlet fever 1,994, whooping-cough 1,206, diphtheria 28, measles 9,178, acute poliomyelitis 101, dysentery 236, paratyphoid fever 8, and typhoid fever 8.

Industrial Accidents and Diseases

The number of workpeople (other than seamen) in the United Kingdom whose deaths from accidents in the course of their employment were reported in September was 120, compared with 81 in the previous month and 106 (revised figure) in September, 1951.

Cases of industrial disease reported during the month were as follows: lead poisoning 1, other poisoning 1, anthrax 2, epitheliomatous ulceration 12, chrome ulceration 5; total 21. One death was reported, from epitheliomatous ulceration.—*Ministry of Labour Gazette*, October, 1952.

Medical News

Medical Women's Federation.—A dinner was held on November 1 at which a company of about 500 was present to celebrate the Federation's 35 years' existence. In proposing the toast of the Federation, Sir Cecil Wakeley, P.R.C.S., said he thought there was not even yet enough equality for women in the medical profession. Surely there should be more than one woman medical officer of health, and there should be more women in charge of maternity and child welfare services. The knowledge derived from their special interests was valuable in teaching, and women could teach on their own subjects as well as, or better than, men. In responding to the toast, Dr. Doris M. Odlum, President of the Federation, emphasized that their Federation had no ideas of separatism from the main body of the profession, and no grievances against their men colleagues. They had received much help and kindness from the B.M.A., and the Association had been 100% loyal in preventing employers

from trying to get women to undercut men, and women doctors had always played fair, too, with the result that the dignity of the medical profession had been enhanced. Women had a special contribution to make to social medicine, and the council of their Federation had often to prepare memoranda on medico-social affairs. There was still, however, a need to watch attempts to make inroads into women's equality with men. In a felicitous speech that included some delicately drawn biographical sketches, Dr. Janet Aitken proposed the health of the guests, who included the Duchess of Northumberland, Mr. A. Gemmell, P.R.C.O.G., Dame Hilda Lloyd, and Miss Patricia Hornsby-Smith, M.P., Parliamentary Secretary to the Ministry of Health. The last responded, and spoke with very real pride of the battle won by women in the medical profession in spite of prejudice in the early days. She shared the President's pleasure that the Federation showed no separatist inclinations, adding that women got along a lot further and a lot quicker when they worked with men and "not agin them." An account of the Federation's two-day congress, of which this dinner was the principal entertainment, will appear in our next issue.

Mr. Iain Macleod's Broadcast.—Health matters were not prominent in Mr. Iain Macleod's party political broadcast on October 30: economics, as appears inevitable in these days, took pride of place. The Minister did say, however, that he welcomed the Government's emphasis on housing, as so many old people—"probably as many as half"—go into hospitals or homes because their housing conditions are intolerable. He also made a plea for more voluntary effort in the National Health Service. "I won't be content till every hospital and institution in the Service has its own voluntary organization, League of Friends, or whatever you may like to call it." Mr. Macleod ended with a graceful tribute to those responsible for our record low infant mortality rates this year.

Tsan Yuk Maternity Hospital.—The present Tsan Yuk Hospital in Hong Kong is now forced to undertake about three times the amount of maternity work for which it is properly equipped. It was originally opened in 1922 with 30 beds, and last year 5,819 babies were born in the hospital and its annexe (a total of 85 beds), with a maternal mortality rate of 1.2 per 1,000. Last week, on October 28, the Duchess of Kent laid the foundation stone of a new Tsan Yuk Hospital, near the existing one. The new hospital, a seven-storied building, will have 200 beds and accommodation for a resident staff of seven doctors, a matron, 28 nurses, 72 pupil midwives, and 88 amahs. There will also be facilities for 12 resident medical students to do their midwifery clerkships. This has been made possible by a generous gift of $3,500,000 from the Hong Kong Jockey Club.

St. George's Hospital Laboratories.—An informal party on October 30 marked the opening of the extensions to the laboratories of St. George's Hospital Medical School. A three-storied building in Knightsbridge adjoining the hospital has been reconstructed and equipped for this purpose. The bottom floor consists of an up-to-date laboratory, provided with bench accommodation for 60 students. The excellent lighting is a special feature of this new accommodation. The middle floor houses the staff of the pathology and experimental pathology departments, and also includes a small extension of the chemical pathology division, and on the top floor there is a virus laboratory, a tissue culture laboratory, and another laboratory devoted to bacteriological chemistry, in addition to individual rooms for the reader and his senior lecturer. All these constitute a new wing. Meanwhile the old laboratories of St. George's are being modernized and brought up to date. Funds for the extensions have been provided by the University of London. The guests on the occasion of the opening included Sir Russell Brain and Sir Cecil Wakeley. They were received by Sir Malcolm Trustram Eve, chairman of the hospital and of the Medical School Council, who has been the moving spirit behind the new enterprise.

Medical School for Gold Coast Postponed.—The commission of inquiry into the health needs of the Gold Coast, appointed last February, has now reported. One of the recommendations in its comprehensive report deals with the establishment of a local medical school. In the Colony's development plan £1,200,000 has been earmarked for a medical faculty at the University College of the Gold Coast. However, the commission of inquiry points out that the number of doctors in the Colony is unlikely to exceed 200 for a considerable time, and that an annual recruitment of 10 would suffice. The commission thinks that it would be extravagant to have a medical school for such a small output, and that it would be less costly to send medical students to Britain for training. The Gold Coast Government agrees with this view.

Royal Commission on Marriage and Divorce.—Representatives of the Church of Scotland, giving evidence before the Royal Commission in Edinburgh on October 29, asked among other things for legislation "to enable sufficient grants from public funds to be made for the secretarial and administrative organization of marriage guidance." This was an amendment by the Church's General Assembly to a recommendation in its *ad hoc* committee's report. The committee had wanted a national marriage guidance service, financed by public funds and "modelled on the lines of a national health service." Explaining to the Royal Commission why the General Assembly had reversed this proposal, the committee's convener, the Very Reverend Dr. J. Hutchison Cockburn, is reported to have said that the Assembly feared State control of marriage guidance would make it rather rigid and detached. A voluntary body would take a wider and perhaps more humane view.

Medicine and the Colombo Plan.—As part of Britain's contribution to the technical co-operation scheme of the Colombo Plan specialist medical teams are being sent to the Far East to help develop medical facilities there. One of these, under Mr. Robert Roaf, a Liverpool orthopaedic surgeon, has just left this country for India, where an orthopaedic unit will be started at a new medical centre in New Delhi. Mr. Roaf, who takes with him two orthopaedic sisters and about £1,000 worth of equipment, will spend two years in India. He will set up a 150-bed orthopaedic hospital, and also undertake graduate and postgraduate teaching. This arrangement has been made possible by the Ministry of Health allowing Mr. Roaf two years' leave of absence; after his tour in India Mr. Roaf will return to his Liverpool appointments.

Consumer Research.—In a letter to *The Times* of November 3 the assistant director of the National Institute of Industrial Psychology, Mrs. Winifred Raphael, says that the Institute is planning systematic surveys of patients' opinions on their treatment in hospital. She suggests that a contented patient may recover more quickly than one who is unhappy or nervous. Before the Institute can undertake any large-scale investigation of this sort outside financial help will be required, as well as the good will of the hospitals concerned.

Libel and Slander.—Mr. Harold Lever's Defamation (Amendment) Bill received the Royal Assent on October 30. All the major recommendations of the Porter Committee (see *Journal*, February 2, p. 266) are retained in the Act.

"Lancet" Staff.—Dr. E. Clayton-Jones has resigned from his position as assistant editor of the *Lancet* because of ill-health. Dr. Clayton-Jones joined the staff in 1938. He is succeeded by Dr. I. Douglas-Wilson.

New Councillors of Royal College of Physicians.—At the quarterly comitia on October 30, Dr. Geoffrey Bourne, Professor E. C. Dodds, F.R.S., Professor Robert Platt, and Dr. J. T. Ingram were elected councillors of the College.

Society of Apothecaries.—Dr. H. Seaward Morley, senior physician to the Royal West Sussex Hospital, has been appointed Senior Warden of the Society, and Sir Cecil Wakeley Junior Warden.

Emergency Bed Service: Applications and Admissions.—During the seven days ending November 3 the number of applications made by doctors to the London Emergency Bed Service for admission of patients was 970, of whom 92.58% were admitted.

Dr. T. Clarence Routley, general secretary of the Canadian Medical Association, was on November 7 awarded the Medal of Honour by the president and members of the Canadian Pharmaceutical Manufacturers' Association "in recognition of his exemplary statesmanship in the field of international medicine." Previous awards have been made to Sir Alexander Fleming, Professor Charles Best, and Dr. Edward C. Kendall.

Dr. Dag Knutson, of Stockholm, has been elected chairman of the Council of the World Medical Association for the coming year in succession to Dr. Pierre Glorieux, of Brussels.

Dr. L. A. Hulst, of Holland, was nominated by the General Assembly of the World Medical Association at Athens last month as president-elect for the session 1953–4.

NEW ISSUES

British Journal of Social Medicine.—The next issue of this journal (Vol. 6, No. 4) will be available in a week's time. The principal contents include:

STATISTICAL THEORY OF PROPHYLACTIC AND THERAPEUTIC TRIALS. II: METHODS OF OPERATIONAL ADVANTAGE. Lancelot Hogben and Raymond Wrighton.

COHORT ANALYSIS OF FERTILITY IN ENGLAND AND WALES, 1939–50. Wallis Taylor.

STATURE OF SCOTSMEN AGED 18 TO 40 YEARS IN 1941. E. M. B. Clements and Kathleen G. Pickett.

INCIDENCE OF NEUROSIS RELATED TO MATERNAL AGE AND BIRTH ORDER. Alan Norton.

FACTORS INFLUENCING SEX DIFFERENCES IN MORTALITY FROM RESPIRATORY TUBERCULOSIS IN ENGLAND AND WALES. J. C. McDonald.

A NOTE ON THE SEX RATIO IN ANENCEPHALUS. Brian MacMahon and Thomas McKeown.

Issued quarterly; annual subscription £2 2s., single copy 12s. 6d.; obtainable from the Publishing Manager, B.M.A. House, Tavistock Square, London, W.C.1.

SOCIETIES AND LECTURES

Details in this column are necessarily brief. Further information and tickets where required (marked ●) should be obtained from the institution concerned.

Monday, November 10

●INSTITUTE OF CHILD HEALTH.—5.30 p.m., Professor T. H. Bosworth: Pathogenesis and Control of Some Diseases of Newborn Animals.

INSTITUTE OF PSYCHIATRY.—4.30 p.m., Dr. E. Stengel: Lecture-demonstration.

LONDON UNIVERSITY.—At London School of Hygiene and Tropical Medicine, 5.15 p.m., Heath Clark Lecture by Dr. H. E. Sigerist (Yale): (1) Galen's Hygiene.

MEDICAL SOCIETY OF LONDON.—8.30 p.m., discussion on Acute Intestinal Obstruction.

PHARMACEUTICAL SOCIETY OF GREAT BRITAIN.—7.30 p.m., Mr. K. R. Capper, Ph.D.: Extra Pharmacopoeia.

ROYAL EYE HOSPITAL.—5 p.m., Professor Arnold Sorsby: Diagnosis of Hereditary Affections.

ROYAL INSTITUTE OF PUBLIC HEALTH AND HYGIENE.—4.30 p.m., Blackham Lecture by Major-General H. C. D. Rankin: Review of Army Health.

Tuesday, November 11

CAERNARVONSHIRE AND ANGLESEY PAEDIATRIC CLUB.—At Clinic, Sackville Road, Bangor, 4.30 p.m., Dr. Mary Sheridan: Neglectful Mothers.

●INSTITUTE OF DERMATOLOGY.—5.30 p.m., Dr. C. O. Carter: Genetics.

LONDON UNIVERSITY.—At London School of Hygiene and Tropical Medicine, 5.15 p.m., Heath Clark Lecture by Dr. H. E. Sigerist (Yale): (2) The Regimen Sanitatis Salernitanum.

MANCHESTER MEDICAL SOCIETY.—5 p.m., Mr H. Bolton: Surgery of the Hand.

ROYAL COLLEGE OF PHYSICIANS OF LONDON.—5 p.m., Charles West Lecture by Professor A. A. Moncrieff: Infection in the Newborn Baby.

WEST END HOSPITAL FOR NERVOUS DISEASES.—5.30 p.m., Dr. G. Parsons-Smith: neurological demonstration.

Wednesday, November 12

HARVEIAN SOCIETY OF LONDON.—8.15 p.m., discussion on Surgery in Pulmonary Tuberculosis.

●INSTITUTE OF DERMATOLOGY.—5.30 p.m., Dr. H. Haber: Diagnosis by Biopsy and Cytology.

●LONDON MARRIAGE GUIDANCE COUNCIL.—6.30 p.m., Dr. P. M. Bloom: Sex Disorders in Marriage.

LONDON UNIVERSITY.—At London School of Hygiene and Tropical Medicine, 5.15 p.m., Heath Clark Lecture by Dr. H. E. Sigerist (Yale): (3) The Quest for Long Life in the Renaissance.

MANCHESTER MEDICAL SOCIETY.—4.30 p.m., Dr. L. Parker and Mr. G. K. Tutton: Cerebral Abscess.

OXFORD UNIVERSITY.—At Radcliffe Infirmary, 5 p.m., Litchfield Lecture by Professor E. E. Pochin: Radioiodine in Thyroid Disease.

ROYAL EYE HOSPITAL.—5.30 p.m., Mr. L. H. Savin: Surgery of the Eyelids, Lacrimal Sac, and Orbit.

ROYAL FACULTY OF PHYSICIANS AND SURGEONS OF GLASGOW.—5 p.m., Weild Lecture by Professor A. C. Frazer: Defective Intestinal Absorption.

Thursday, November 13

ALFRED ADLER MEDICAL SOCIETY.—At 11, Chandos Street, Cavendish Square, W., 8 p.m., Dr. T. A. Werner: Psychodynamics in Psychotherapy.

HONYMAN GILLESPIE LECTURE.—At University New Buildings, Edinburgh, 5 p.m., Dr. I. Simson Hall: Cancer of the Larynx.

●INSTITUTE OF DERMATOLOGY.—5.30 p.m., Dr. R. W. Riddell: Mycology—Skin Infections due to Yeast-like Organisms.

●INSTITUTE OF OBSTETRICS AND GYNAECOLOGY.—At Hammersmith Hospital, Ducane Road, W., 2 p.m., Dr. J. D. N. Hill: Puerperal Insanity.

LIVERPOOL MEDICAL INSTITUTION.—3 p.m., Hugh Owen Thomas Memorial Lecture by Mr. A. Rocyn-Jones: Treatment of Joint Tuberculosis. 8 p.m., annual dinner.

LONDON UNIVERSITY.—At London School of Hygiene and Tropical Medicine, 5.15 p.m., Heath Clark Lecture by Dr. H. E. Sigerist (Yale): (4) John Peter Frank (1745-1821), Pioneer in Social Medicine.

ROYAL COLLEGE OF SURGEONS OF ENGLAND.—5 p.m., Imperial Cancer Research Fund Lecture by Professor M. J. Stewart: Synovial Tumours.

ROYAL EYE HOSPITAL.—5.30 p.m., Miss M. Savory: Newer Therapeutic Measures.

ST. ANDREWS UNIVERSITY.—At Materia Medica Department, Dundee, 5 p.m., Mr. T. McW. Millar: Chronic Ulcerative Disease of the Colon.

ST. GEORGE'S HOSPITAL MEDICAL SCHOOL.—5 p.m., Dr. M. A. Partridge: lecture-demonstration in psychiatry.

Friday, November 14

●INSTITUTE OF DERMATOLOGY.—5.30 p.m., Dr. R. T. Brain: Epithelial Tumours.

LONDON UNIVERSITY.—At London School of Hygiene and Tropical Medicine, 5.15 p.m., Heath Clark Lecture by Dr. H. E. Sigerist (Yale): (5) The Changing Pattern of Medical Care.

ROYAL EYE HOSPITAL.—4.30 p.m., Mr. A. J. Cameron: Red Eye and its Differential Diagnosis.

ROYAL MEDICAL SOCIETY, Edinburgh.—8 p.m., Mr. H. S. Tinniswood: Enuresis.

Saturday, November 15

BIOCHEMICAL SOCIETY.—At London School of Hygiene and Tropical Medicine, Keppel Street, W.C., 10.30 a.m., symposium: Immunochemistry.

APPOINTMENTS

Dr. S. H. O. Jones has been appointed an Appointed Member of the Executive Council of the Gambia.

ARDLEY, JOHN, M.B., B.S., D.P.H., Deputy Medical Officer of Health and Deputy School Medical Officer, County Borough of Southport.

HOLLIS, P. W. T., M.B., B.S., Assistant Medical Director, Mass Radiography Units at Bristol, South-western Regional Hospital Board.

HOSPITAL FOR SICK CHILDREN, Great Ormond Street, London, W.C.—*Senior Ear, Nose, and Throat Registrar*, A. W. Halfhide, M.B., B.Ch., D.L.O. *Assistant Medical Registrars*, Constance C. Forsyth, M.B., Ch.B., M.R.C.P., K. Hugh-Jones, M.D., M.R.C.P. *Junior Resident Anaesthetists*, Myer Rooms, M.B., B.S., Jean M. Horton, M.B., B.S. *House-physicians*, D. A. McGreal, M.B., Ch.B., M.R.C.P., D.C.H., J. A. C. Wilson, M.B., Ch.B., M.R.C.P., K. S. Holt, M.D., M.R.C.P. *House-surgeon to the Orthopaedic and Plastic Departments*, D. J. Stephens, M.B., Ch.B. *House-surgeon*, B. T. Smyth, M.B., B.Ch., B.A.O., F.R.C.S.

WATT, JAMES, M.B., Ch.B., Lecturer in Pathology, University of Liverpool.

BIRTHS, MARRIAGES, AND DEATHS

BIRTHS

Roffey.—On October 7, 1952, at Sydney, Australia, to Jean, wife of Surgeon Lieutenant E. H. Roffey R.A.N., a daughter—Ann Elizabeth.

MARRIAGES

Fleming—Phelan.—On October 4, 1952, at Glanmire, Co. Cork, Alan Chalmers Fleming, M.B., B.S., to Maureen Phelan, M.B., B.Ch.

DEATHS

Andrew.—On October 14, 1952, at 15, Howell Road, Exeter, Henry Andrew, M.R.C.S., L.R.C.P., aged 86.

Aspinwall.—On October 11, 1952, Guy Richmond Aspinwall, L.M.S.S.A., of Ingfield House, Marsden, Huddersfield, Yorks.

Dawson.—On October 16, 1952, in a Colwyn Bay nursing-home, Charles Hollows Dawson, M.B., Ch.B.

FitzGerald.—On October 15, 1952, at Porters Lea, Shenley, Herts, John Joseph FitzGerald, M.D., aged 83.

Hay.—On October 17, 1952, at 555, Lincoln Road, Peterborough, William Peach Hay, M.B., C.M., aged 82.

Hunt.—On October 17, 1952, at The Barn House, Church Handborough, Oxon, Mary Helen Carew Hunt (formerly Cruickshank), M.D.

Knapp.—On October 13, 1952, at Godalming, Surrey, Montague Henry Knapp, M.R.C.S., L.R.C.P., Surgeon Captain, R.N., aged 84.

McCredie.—On October 10, 1952, at Ailsa, Stranraer, Peter Aitken McCredie, M.B., F.R.C.S.Ed., aged 59.

Morris.—On October 14, 1952, at 27, Okehampton Close, London, N., John Mudie Morris, M.B., C.M., D.P.H., formerly of Neath, Glam, aged 86.

Perram.—On October 16, 1952, at Overstowey, Teignmouth, Devon, Edward Arthur Perram, M.D., aged 88.

Smyth.—On October 13, 1952, in hospital, William James Smyth, M.B., B.Ch., D.P.H., of "Innisfail," Boroughbridge Road, Northallerton, Yorks.

Talent.—On October 17, 1952, at Newlands, Grange-over-Sands, Lancs, John William Talent, M.D.

Any Questions?

Correspondents should give their names and addresses (not for publication) and include all relevant details in their questions, which should be typed. We publish here a selection of those questions and answers which seem to be of general interest.

Prolapse in a Young Mother

Q.—*What treatment is advised for complete prolapse of the uterus in a young mother of two children who wishes to increase her family? Is operation likely to interfere with child-bearing?*

A.—The best treatment is by some form of vaginal repair operation. Even if a pessary will give relief it is usually wrong to condemn a woman to the pessary life when she is in her most active years. The important point in the operative treatment is to avoid removing the cervix, if this is at all possible. If the cervix is removed, fertility may be lowered, there is a tendency to abortion and premature labour, and the next delivery is occasionally complicated by difficulty in dilatation or tearing of the os uteri. If the cervix is not removed then further child-bearing should not be affected except that the scars in the vagina and perineum may resist stretching. This can be circumvented by extensive episiotomy, which should in any case be carried out in the next delivery to minimize the chance of recurrence of prolapse.

Local Chloramphenicol and Aplastic Anaemia

Q.—*Can locally applied chloramphenicol, as in the treatment of blepharitis, give rise to aplastic anaemia or so sensitize a person that later parenteral therapy will do so?*

A.—There is no evidence that any such effect can occur: all published cases of aplastic anaemia due to chloramphenicol have received the drug by mouth. It is presumably necessary for a substantial amount to reach the bone marrow *via* the blood stream, and the quantity absorbed after application to so small an area would be trivial.

The Frontal Lobes

Q.—*What is the current view of the functions of the frontal lobe of the brain in man?*

A.—The functions of the frontal lobe, with the exception of the motor and premotor cortex, are not directly known. We can only make a guess from the results of injury or disease. A large amount of information from this point of view has accumulated from the operation of leucotomy. In the modified forms of this operation which are now usual, the degree of damage or disability suffered after operation is often minimal, even too small to be recognized by the clinician. Where it is apparent, it is shown by a tendency to short-circuit reactions in behaviour, the shortening of duration of emotional changes, shallowness of effect, increased egoism, and diminished regard for others, etc. From this one might presume that the function of the silent regions of the frontal lobe is to elaborate and integrate affective responses with the other modes of response of the individual to the environment, so as to secure an emotionally harmonious life. This is, of course, a psychiatric rather than a physiological way of putting the matter. In more physiological terms, Denny Brown has regarded the function of the frontal lobe as essentially concerned with attention to stimuli, perhaps particularly visual attention. If attention is impaired, present stimuli are not correlated with past experience and the individual lives in the present and becomes the victim of reactions to concrete experiences, abstract factors which should influence behaviour being left out of account.

Insanity and Marriage

Q.—*Advice is sometimes sought about the risks of marrying into a family where there is insanity. What factors are relevant in giving such a prognosis? Have any types of insanity either a specially good or specially bad reputation so far as inheritance is concerned? Can any estimate be given of the magnitude of the risk compared with that in a marriage where there is no history of serious mental illness on either side?*

A.—The risks to be considered are those affecting the spouse from the family in which there is insanity, and those affecting any possible children of the marriage. A great number of factors have to be taken into consideration: the nature of the insanity and the clinical details of the psychosis in the affected relative, the closeness of the relationship between this relative and the spouse, the personalities of both these persons and of other members of the family, the age at which the psychosis appeared in the one and at which marriage is being contemplated in the other, the personality and family history on the side of the other contracting party, the extent to which children are desired, etc. The risks have to be entirely differently assessed in different mental disorders, and in such conditions as schizophrenia, manic-depression, presenile dementia, etc., quite different prognoses would have to be given.

For the average member of the population the risk of treatment in a mental hospital at some time during life can be assessed as about 4%. For an individual coming from a family in which no case of mental illness in any relative, near or remote, is known, the risk would be substantially less. On the other hand, the risk of Huntington's chorea in the child of a Huntington choreic, to take an extreme example, is about 40%.

The Binaural Stethoscope

Q.—*Who invented the binaural stethoscope?*

A.—The exact date of the first binaural stethoscope is not known. Laennec first improvised a monaural instrument from rolled sheets of papers on September 13, 1816. The next form was probably the simple straight tube. Piorry reduced the stem to finger-thickness and added an earpiece and a trumpet-shaped chestpiece. These instruments were made of wood. According to Sir Robert Young[1] the flexible stethoscope was introduced by N. P. Comins[2] in 1829, who suggested that it might be made so that both ears could be used—the first suggestion of the binaural instrument. In the *British Medical Journal* (1907, 2, 6) C. Theodore Williams described a stethoscope which he claimed was invented by his father, C. J. B. Williams (1805–89), in 1829. (Williams senior studied for a time under Laennec.) This instrument consisted of a trumpet-shaped mahogany chestpiece, the end of which was screwed into a connexion to which were attached two bent lead pipes (india-rubber not then being available). These pipes could be adjusted to the ears but had no earpieces or fittings of any kind and were difficult to apply. Dr. Arthur Leared showed an improved form at the International Exhibition of 1851, with tubes of gutta-percha. N. B. Marsh, of Cincinnatti, described a binaural stethoscope in the same year, and about that time another American, G. P. Cammann, invented what must be the first stethoscope of the modern type, with metal tubes, spring, rubber tubes and chestpiece. C. J. B. Williams[3] recorded in his *Memoirs* his improvement in the form of a trumpet-shaped expansion for the pectoral end of the monaural form, which he had first described in 1842.[4] He wrote: "This is the form of stethoscope which I have used ever since, with entire satisfaction." He again described this stethoscope in a paper "On the Acoustic Principles and Construction of Stethoscopes and Ear Trumpets" read to the Royal Medical and Chirurgical Society[5] in 1873, but he made no reference in it to the binaural instrument. Williams continued: "At the meeting . . . at which my paper was read" (i.e.,

1873) "I had the opportunity of showing to the late Dr. Leared that I had anticipated him in the invention of a binaural stethoscope; but his was much better than mine, through the addition of an india-rubber spring. The binaural instrument has some advantages in facility of application; but it by no means transmits the chest sounds so simply, or faithfully, as the straight tube. I could never avail myself of its use; for during the last 20 or 30 years, the hearing of one ear has been defective. I have found the same to be the case with many of my brother auscultators." Sir Robert Young's presidential address to the Medical Society of London[1] is a comprehensive account of the early history of the stethoscope.

REFERENCES

1 *Trans. med. Soc. Lond.*, 1931, **54**, 1.
2 *Lancet*, 1828-9, **2**, 685.
3 *Memoirs of Life and Work*, London, *Smith, Elder*, 1884, p. 49.
4 *Lond. med. Gaz.*, 1842, **1**, 401.
5 *Proc. roy. med. chir. Soc.*, 1873, **7**, 189.

Barrier Creams in Industry

Q.—*What non-proprietary barrier creams are advised for industrial use? How effective are they against (a) chemical irritants and (b) physical irritants such as glass, dusts, etc.?*

A.—The "barrier cream" advised for industrial use on the most general basis is a mixture of anhydrous lanolin (65 parts) with castor oil (35 parts). This resists aqueous solutions to some extent, assists in washing, and is an emollient. An aqueous jelly (e.g., tragacanth–water mixture with 5% glycerin) is one of many alternatives. The effectiveness of barrier creams is limited unless special attention is paid to the particular working conditions and to general hygienic considerations. Irritant powders, for instance, may adhere to a cream more than to untreated skin, though this may be avoided by powdering with talc after application. In some chemical processes mild irritants have been successfully resisted by careful choice of barrier (sometimes containing specific neutralizing or detecting agents) together with accessory measures, especially if these are fully explained to a co-operative group of workpeople. Mechanical irritants can seldom be neutralized in this way, though the use of emollients after washing at the end of shifts may prevent minor surface abrasions leading to serious cracking and infection.

Acetone Poisoning and Immobilizing Casts

Q.—*A boy of 3 years of age was anaesthetized with open ether for the purpose of applying a "glassona" single-leg spica to immobilize a tuberculous knee-joint. He woke within 20 minutes of completing the cast, but one hour later relapsed into unconsciousness and remained unconscious for the next 18 hours. While his colour was good, his respirations were shallow and his pulse rapid. His temperature rose to just over 100° F. (37.8° C.). He was given rectal saline and kept under observation. The following morning he was awake and seemed none the worse, but his urine was loaded with acetone. The fluid used to set the cast consists almost entirely of acetone. Is this an example of acute acetone poisoning, either from inhalation or from absorption through the skin?*

A.—Acetone is a narcotic, but it is used in enormous quantities in industry and authentic cases of acute poisoning have only been rarely recorded. The hazard in industry arises from exposure to the vapour. Under ordinary circumstances the risk of penetration through the skin does not arise, because of the volatility of acetone. Splashes on the skin or clothes will dry by evaporation before penetration can be effected. Whether such penetration can take place under the special conditions described is not known. Elsewhere in this issue Drs. L. C. Harris and R. H. Jackson (p. 1024) record a rather similar case, and have found three others in the literature. In addition Dr. Ethel Browning, in *Toxicity of Industrial Organic Solvents* (Industrial Health Research Board Report No. 80, p. 316), cites an earlier case.

"The case reported by Cossmann (*Münch. med. Wschr.*, 1903, **50**, 1556) is unique in the literature. If accepted as a true case of acetone poisoning it would indicate that this substance can be absorbed through the skin in sufficient quantities to exert a narcotic effect. The patient was a 12-year-old boy suffering from a tubercular hip, to which after long immobilization a plastic bandage of 'celluloid mull' made with acetone was applied. Within 24 hours he exhibited symptoms similar to those of diabetic coma—mydriasis, dilatation of the pupils, small pulse, deep slow respiration and sleep of 24 hours' duration. Acetone was present in the urine, the vomit, and the expired air. An attempt to reproduce the condition in a dog by a similar application was only partly successful, the dog became semi-narcotized, but no acetone was present in the urine."

NOTES AND COMMENTS

Children's Ankles.—Mr. E. I. LLOYD (London, W.1) writes: I think it is a pity that your expert ("Any Questions?" October 4, p. 790) does not mention knock-knee, as I believe that this deformity is caused in the great majority of instances by the weak valgus ankles which are the subject of the question. Unfortunately, the belief that rickets is the common cause of knock-knee dies hard, and may even survive the disease itself. Valgus ankles are very common in children, but a true flat foot is very rare and in some instances (possibly all) is associated with a bone abnormality which seems to bear no relationship to the inadequate tibial muscles of valgus ankles. These are, I submit, completely different conditions, but the treatment of valgus ankles (such as it is) still remains the preventive surgery of knock-knee.

Dr. J. H. CYRIAX (London, W.1) writes: Your expert's reply ("Any Questions?" October 4, p. 790) on valgus heels in children omits the commonest cause of this condition. This is unfortunate, since simple and effective treatment exists. The disorder was described and illustrated as "metatarsus inversus,"[1] and discussed under the name of varus forefoot by Professor G. Perkins[2] in his presidential address to the Section of Orthopaedics of the Royal Society of Medicine. If the forefoot is medially rotated on the hindfoot, the outer border of the foot reaches the ground first. Then, as the child's weight comes on to it, the forefoot has to rotate laterally until the sole is flat on the ground; it carries the hindfoot with it, forcing the heel into valgus at the talo-calcanean joint. Exercises to the tibial muscles increase the deformity; wedged heels increase the child's difficulty in walking. Manipulation of the mid-tarsal joint in due course restores parallel. After Professor Perkins's presidential address, Sir Thomas Fairbanks pointed out that this common deformity was not mentioned in orthopaedic textbooks; it is therefore important that its recognition and cure should be widely stressed.

REFERENCES

1 Cyriax, J. (1947). *Rheumatism and Soft Tissue Injuries*. Hamish Hamilton, London.
2 Perkins, G. (1948). *Proc. roy. Soc. Med.*, **41**, 31.

Sixth Nerve Palsy after Spinal Anaesthesia.—Mr. R. FOSTER MOORE (Salisbury) writes: In your reply ("Any Questions?" October 11, p. 842) as to the cause of the above, no mention is made of Harvey Cushing's explanation, which seems to me more convincing than any other. He points out that, as the sixth nerve runs directly forwards from the hind margin of the pons, it is crossed, ventrally and at right angles, by either, or both, the anterior inferior cerebellar and internal auditory arteries, so that, should swelling of the cerebellum occur, these arteries are stretched and, being anchored below to the basilar, may cut into the nerve like an india-rubber band; if you will look at the section he publishes you may, I think, find it convincing. I should have thought the paralysis came on within 24 hours; the shortest time in which I can be sure of having seen recovery is 14 days.

Correction.—Discussing immunization against poliomyelitis in the *Journal* of September 6 (p. 551), we referred to the Lansing immunological type as the most virulent. This should have been the Brünhilde.

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